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SOME ASPECTS OF ALCOHOL IN BODY FLUIDS. PART I: CORRELATION BETWEEN BLOOD ALCOHOL CONCENTRATION AND ALCOHOL CONSUMPTION.

By N. E. W. McCALLUM

AND

J. G. SCROGGIE,

Laboratory of Forensic Science, Department of Pathology, University of Melbourne.

IN recent years, chemical tests on various body fluids have proved an increasing aid in determining the condition of motorists suspected of driving while "under the influence of alcohol". In Australia, blood has been used mainly for this purpose, and this paper will be confined almost exclusively to this test. In England, urine seems to be preferred (British Medical Association, 1958), while breath analysis has become important recently in the United States; the results of these two tests are commonly expressed in terms of a corresponding blood alcohol concentration.

Despite the widespread use of such tests, it is apparent that widely divergent views exist in charges of "driving under the influence" on the evidential value of a blood alcohol analysis. On the one hand, the opinion is expressed that the value of the blood test, for this purpose, is exceedingly limited—or even negligible—while, on the other, it is maintained that the blood test is the complete answer to this question.

One factor apparently thought to limit the value of the blood test is the impossibility, by its application alone, of describing accurately the degree of intoxication produced in any particular individual. This view has been expressed by Smith and Glaister (1939), who state that "chemical analysis of blood, urine, or expired air, does not yield information on which, alone, a diagnosis of alcoholic intoxication can be made or rejected". More recently, Glaister (1957) confirmed this view, although he corrected the foregoing statement in so far as rejection of intoxication is concerned when no alcohol is present. Glaister states:

> From these estimations the probability, or otherwise, of intoxication being present can be gauged, but the estimation by itself cannot always be taken as a certain indication that a condition of insobriety exists... If no alcohol can be demonstrated in the blood or urine there can be no alcoholic intoxication present.

A special committee of the British Medical Association in England expressed a similar view in 1958 (British Medical Association, 1958); in England the position of the blood test is clearly defined, and the "clinical examination, in most cases, must remain the determining factor in arriving at a final diagnosis [of intoxication], and the laboratory observation should be

considered as an adjuvant" (Glaister, 1957). However, as will be discussed, it cannot be implied from such statements that the blood test is without value.

Apart from the views on the limitations of a blood alcohol analysis, those who contend that the test is a complete answer to the problem might have difficulty in reconciling such conflicting statements as the following:

> Leaving out for the time being the question of toleration or habituation, we can say that there is world unanimity that at a level of blood alcohol between 30 and 40 milligrammes *per centum* the vast majority of individuals, including those accustomed to take alcohol regularly, can be shown by a large variety of tests, including driving tests, to have mental impairment of such a degree as to be legally and medically 'under the influence' ". (Hansman, 1953.)

> Between 120 and 180 milligrams alcohol per 100 millilitres blood, about 50 per cent of individuals will probably be sober, while over 180 milligrams per 100 millilitres blood will probably indicate intoxication. (Glaister 1950.)

> Where there is over 150 milligrammes per 100 millilitres of blood (0·15 per cent) the amount of alcohol consumed to acquire this concentration will almost always produce intoxication. (Glaister, 1957.)

While the observations of these experts are contradictory and further suggest the limitations of the blood test as the sole guide in a diagnosis, it is, of course, important to examine such publications closely to determine whether the condition of either intoxication or "under the influence of alcohol" is being discussed. For example, Jetter (1938) examined 1159 patients in hospital for alcoholic intoxication and adjudged 83% as intoxicated at a concentration of 0·20%. However, the criteria demanded by Jetter might reasonably be regarded as indicating an advanced degree of intoxication.

If the application of the blood test for alcohol is limited in the above-mentioned sense, it is essential to determine precisely what information the test can provide. Before the use of the test in this country, a common defence to the charge of "driving under the influence" was that the suspected person had taken only "two or three small beers", which would account for any odour of alcohol detected. In addition, it could be claimed that a "black-out" on the part of the driver was responsible for any aberration observed in his driving. At that time, there was no direct means available either for demonstrating the truth of this statement or for testing its validity. The courts were therefore without a reliable guide on this point. The gradual introduction of blood tests, on a voluntary basis, in this State made this type of defence less common. It became evidently difficult for a person having an alcohol concentration of, say, 0·250% in the blood to maintain successfully that he had consumed only a small amount of alcohol.

The foregoing application appears to be one of the most valuable aspects of the analysis of a blood sample for alcohol, and the information to be derived from such an analysis may be broadly summarized as follows. (*a*) Alcohol is, or is not, present in the sample, i.e., the subject has, or has not, been drinking. (*b*) From the amount of alcohol found by analysis, it is possible to calculate the minimum amount of alcohol which would normally be consumed to reach this concentration.

While the results of an analysis may be unfavourable to the case of a person who has been drinking heavily and is charged with driving a car while under the influence of alcohol, the test is also the motorists' greatest protection against being wrongly presented on this charge. For example, if a driver who has taken only one or two glasses of beer shows symptoms, after an accident, which simulate those of alcoholic intoxication, the analysis of a blood sample will confirm the accuracy of the driver's account of his drinking.

Therefore, the blood test has a proper place in evidence in countries where it is an offence for a person to operate a motor vehicle while "under the influence of intoxicating liquor to such an extent as to be incapable of having proper control of it". In the State of Victoria, for instance, the legislation provides (*Victorian Crimes Act*, 1957) for the admission of evidence of a chemical analysis of the blood of a person suspected of driving under the influence of alcohol, but no special significance is given to the result of such analysis except that, below a concentration of 0·05%, the concentration is admissible as *prima facie* evidence of innocence. Above this figure, the result of the analysis is admissible together with all other "relevant and admissible" evidence, and the Court reaches its decision by a consideration of all such evidence.

Other legislating bodies have extended the application of the test so that it becomes almost the sole factor in determining the innocence or guilt of a person. About twenty years ago, legislation was enacted in the United States which recognized three separate zones of alcohol concentration in the blood, and similar legislation has been introduced recently in Western Australia. In this, a concentration of below 0·05% is admissible as *prima facie* evidence that a person was not intoxicated, whereas a concentration above 0·15% is admissible as *prima facie* evidence that the person was intoxicated; in the intermediate zone, the alcohol concentration is contributory evidence only. An objection has been raised to this type of legislation on the grounds that, at a concentration of 0·150%, not all persons will be "under the influence" or intoxicated. On this proposition, then, the law recognizes *prima facie* evidence based on a premise which is not true in all cases. Whatever the merits of this objection, such legislation has operated in the United States for many years.

Another form of legislation, originally introduced in the Scandinavian countries, was the establishment of an upper permissible limit of alcohol in the blood of motorists. Thus it became an offence for a person to drive a car when his blood alcohol concentration was above, say, 0·100%. The objection often raised to this form of legislation is that all are grouped under the one concentration limit and no account is taken of variation of response to alcohol in different people; according to this, the "good drinker" is penalized. This has been countered by comparing such legislation with that for a speed limit, in which a restriction is placed upon good and poor drivers alike. The legislation is not based on the proposition that, at the concentration limit fixed, all persons would necessarily be "under the influence" or intoxicated, but rather that a sufficiently large percentage of people would be so affected by alcohol that it is undesirable for any driver to be allowed to operate a car above this concentration.

It has been suggested that the last two types of legislation can operate successfully only if there is some procedure whereby a person may be compelled by law to provide a sample of blood (or other body fluid) for analysis. This point is, of course, beyond the scope of the present discussion, but it does serve to illustrate further the complexity of the problem.

The aim of the work described below was to determine the concentration of alcohol added to the blood of a number of different subjects after the consumption of definite amounts of alcohol. In this way, the method for calculating the least amount of alcohol which would normally be needed to attain any given blood alcohol concentration could be derived. Subsequent papers will deal with certain other aspects of the blood test.

Experimental Studies.

In these experiments, the alcohol concentrations reached in the blood of 54 male subjects were recorded after the consumption of definite amounts of alcohol. As it was desired that the absorption of ingested alcohol into the blood should be as rapid and complete as possible, the drinking was begun approximately three hours after only a light meal; the subjects had usually abstained from alcohol for at least twelve hours before testing. A urine sample was obtained from each subject immediately before the experiment began and, where no alcohol was detected by analysis, the blood alcohol con-

centration was presumed to be zero; when alcohol was present in the urine, the subject was included in the experiment, but the results were not acceptable for this particular investigation. Although a blood sample would have been preferred for this initial check, urine specimens were used for the comfort of the subjects, as four blood samples were later collected from each. In some of the later experiments, a further initial check was performed by breath analysis.

In all experiments, the liquor used was beer with an alcohol concentration found to be 5% (v/v), and this was dispensed in seven-ounce units. The subjects drank at their fastest possible rate for a selected time; the rate was so rapid that, in several cases, vomiting occurred and results from these are not included. Where the rapid rate could not be maintained for the desired time, drinking was discontinued and the subject was tested immediately. It should be emphasized here that the subjects varied widely in their drinking habits and ranged from near-teetotallers to heavy drinkers.

A blood sample was taken from each subject within a few minutes after the completion of drinking, and three further samples were collected at intervals up to a period of approximately two hours after drinking. As indicated in Table I, the maximum concentration of alcohol in the blood was reached within this time in all cases. Where possible, a urine sample was collected at approximately the same time as each blood sample, and the volume of urine voided was noted.

TABLE I.
Results.

Subject.	Weight. (Pounds.)	A.	Drinking Time. (Minutes.)	$c_{max.}$	$t_{max.}$	$E_{max.}$
2	124	8	45	0·099	60	0·0124
3	124	6	45	0·100	20	0·0167
4	127	10·5	57	0·153	77	0·0146
5	134	4	34	0·052	60	0·0130
6	135	7	58	0·091	60	0·0130
8	140	8	30	0·090	75	0·0112
9	141	10	55	0·120	34	0·0120
10	141	11	60	0·149	50	0·0135
11	145	10	30	0·138	90	0·0138
12	151	8	20	0·101	90	0·0126
14	154	10·5	75	0·105	80	0·0100
15	154	14	71	0·159	67	0·0114
16	154	7	75	0·095	20	0·0136
17	156	8	30	0·082	90	0·0102
18	156	9	93	0·107	45	0·0119
19	157	6	30	0·070	60	0·0117
20	157	12	60	0·166	38	0·0138
21	158	14	60	0·172	60	0·0123
22	158	14	60	0·164	53	0·0117
23	162	4	30	0·042	45	0·0105
24	168	12	60	0·138	45	0·0115
25	168	9	32	0·096	100	0·0107
26	170	17	60	0·199	67	0·0117
27	171	8	30	0·071	75	0·0089
28	171	10	60	0·147	87	0·0147
29	172	12	60	0·128	55	0·0105
30	174	16	60	0·173	45	0·0108
31	174	12	60	0·124	85	0·0103
33	174	13	60	0·157	55	0·0121
34	175	12	57	0·098	90	0·0082
35	175	14	70	0·165	52	0·0118
36	175	15	60	0·205	45	0·0137
37	175	8	35	0·093	85	0·0116
38	175	15	60	0·164	114	0·0109
39	177	12	59	0·156	75	0·0130
40	177	8	33	0·090	107	0·0112
41	182	8	20	0·092	110	0·0115
43	187	10	60	0·114	36	0·0114
44	188	15	60	0·202	58	0·0135
45	188	12	30	0·115	51	0·0096
46	189	12	30	0·107	90	0·0089
48	190	16	60	0·187	75	0·0104
49	196	23	103	0·254	90	0·0110
50	196	6	20	0·078	38	0·0130
51	196	19	60	0·218	60	0·0115
52	197	21	60	0·208	45	0·0099
53	199	9	60	0·094	60	0·0104
54	206	8	35	0·078	75	0·0097
55	210	12	60	0·111	56	0·0092
56	217	16	60	0·160	51	0·0100
57	217	13	90	0·134	35	0·0103
58	218	14·5	60	0·152	46	0·0105
59	228	9	30	0·073	30	0·0081
60	259	18	60	0·174	75	0·0097

Blood and urine samples were analysed by the method of Kozelka and Hine (1941), which was found to be the most accurate and reliable; standard alcohol solutions could be consistently analysed to within 0·005%.

Results.

The results obtained in the experiments are summarized in Table I. This table records the following facts. (i) The weight (pounds) of each subject. Each subject was allotted a number which was retained throughout this and subsequent experiments. Reasons for the absence of particular subject numbers are discussed above. (ii) The number of seven-ounce glasses of beer (A) consumed. (iii) The time taken for drinking (minutes). (iv) The maximum concentration (c_{max}) of alcohol appearing in the blood (expressed in grammes per 100 ml. of blood. (v) The time taken (t_{max}) after the finish of drinking to reach c_{max} (minutes). (vi) The amount of alcohol (E_{max} — expressed in grammes per 100 ml. of blood) appearing in the blood at the maximum concentration for the consumption of each seven-ounce glass of beer, i.e., $E_{max} = c_{max}/A$.

Discussion.

It has been found that, for 54 different experimental subjects ranging between 119 and 259 lb. in weight, the value of E_{max} has varied from 0·0081% to 0·0167%. When the experiment was repeated in some cases under similar conditions, the appropriate E_{max} values were not significantly altered. It should be stressed that the experiments were designed to produce, from the amount of liquor consumed, the maximum alcohol concentration in the blood, and hence the highest value of E_{max} for each subject. Thus, the rate of absorption of alcohol into the blood would be at a maximum, since all subjects drank at their maximum rate and had taken no food for approximately three hours. Furthermore, the E_{max} values were always calculated from the highest concentration of alcohol appearing in the blood after drinking.

Examination of the results reveals the following features: (*a*) The majority of E_{max} values fall within the range 0·011% to 0·013%; the average value of E_{max} is 0·0115%. (*b*) With one exception, all values of E_{max} lie below 0·015%. The significance of the exceptional value (which was duplicated) will be discussed below. (*c*) When the values of E_{max} are plotted against the weights of the various subjects (Figure I), it is seen that a "scatter" is obtained and there is no simple relation between the values; clearly, a smooth curve cannot be drawn through the points. For example, the graph shows five subjects who have the same weight (175 lb.), but who have E_{max} values of 0·0082%, 0·0109%, 0·0116%, 0·0118% and 0·0137%. (*d*) Although no uniform relation between the variables is evident, there is a significant trend in the values of E_{max} and weight. Thus, in general, a low value of E_{max} tends to be associated with a high weight, and a high E_{max} value with a low weight. The effect is more apparent if the extremes of weight are considered, rather than a narrow weight range.

As current Victorian legislation places no special legal significance on a blood alcohol concentration above 0·05%, it has been our practice to interpret the results of an analysis in terms of the least amount of beer which would normally be required to reach the particular concentration. This figure is referred to a man of medium build and weight (approximately 11 to 12 stone) and, for this purpose, a concentration of 0·015% is used to represent the amount of alcohol added to the blood by the consumption of one seven-ounce glass of beer. Thus a blood alcohol concentration of 0·150% would be equivalent to a minimum consumption of ten seven-ounce glasses of beer. It should be noted that the figure obtained simply represents the equivalent of the amount of alcohol actually circulating in the blood at the time the sample was taken, and does not refer to the period of time over which the drinking occurred. However, as indicated below, a relatively short drinking time is implied in the calculation.

Although this interpretation is used for illustrative purposes and is not intended to apply to any particular individual, the figure obtained is regarded as a minimum in the general case for the following reasons. (i) It is assumed that drinking has not been prolonged. It is clear that, if a person has been drinking over several hours, the elimination mechanism in the body will have removed the alcohol equivalent of several glasses of beer. The rate of elimination of alcohol from the blood is at present under investigation. (ii) It is assumed that the sample was taken when the alcohol concentration was at a maximum; if this is not so, the amount consumed will be further understated. (iii) Even if condition (ii) and the extreme conditions of the present experiments are fulfilled, it will be seen from Table I that, by the use of a standard of 0·015% to represent one seven-ounce glass of beer, the consumption of 53 of the above 54 subjects will be understated, in some cases grossly so.

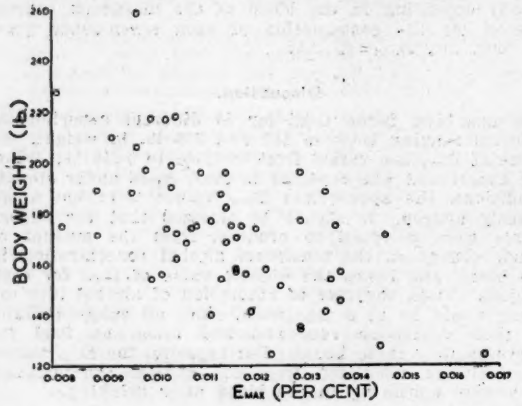

FIGURE I.
Graph of body weight of subjects against their E_{max} values.

Although this appears to be the first detailed Australian report relating blood alcohol concentrations with an amount of liquor consumed, such correlations have appeared in a number of overseas reports. These overseas interpretations are usually based on the Widmark expression:

$$a = r \cdot p \cdot c \cdot$$

in which a is the total amount of alcohol present in the body at any given time after the establishment of alcohol equilibrium, r is the Widmark "individual factor", defined as the ratio between the concentration of alcohol in the whole body and the concentration in the blood, i.e., $r = C_{body}/C_{blood}$, p is the body weight of the particular individual, and c is the blood alcohol concentration at the particular time.

The factor r has been quoted as ranging between 0·60 and 0·85 in males, with an average value of 0·68 (Nickolls, 1956). Calculations of the amount of liquor equivalent to any particular blood alcohol concentration thus depend on the value of r chosen and, for this reason, there is some variance between those interpretations based on the Widmark expression. For example, a value of 0·60, as chosen by Glaister (1957) and the British Medical Association Committee (1958) will provide a lower alcohol equivalent a than the value of 0·70, which has been recommended by Nickolls (1956); the present interpretation of blood alcohol concentrations is in good agreement with the appropriate figure derived from Nickolls's calculations.

It should be noted that use of the Widmark expression again only provides a calculation of the least amount of alcohol circulating in the body at the particular time, and not, as claimed by some, the amount of alcohol actually consumed. Since alcohol destruction begins in the body almost immediately after it is first consumed, the amount of alcohol present in the tissues at any time will always be less than the amount consumed. According to Widmark, the total amount of alcohol consumed (A) is given by the modified expression:

$$A = r \cdot p \cdot (c_t + \beta \cdot t)$$

in which c_t is the blood alcohol concentration at time t after the beginning of drinking, and β is the rate of decrease of blood alcohol concentration.

Some confusion appears to exist in the literature concerning the significance of the Widmark r factor. Thus, for example, this factor has been quoted as varying, in males, "between 0·60 and 0·76 for spirits, while for beer it is about 1·0" (British Medical Association, 1958). However, r is a physiological factor governed by the distribution of alcohol throughout the various bodily tissues (see foregoing definition), and may be derived from the expression:

$$r = A/p(c_t + \beta \cdot t)$$

It is therefore difficult to see how r can be dependent on the type of liquor consumed. Furthermore, since, after equilibrium, the concentration of alcohol in the body as a whole will always be less than the blood alcohol concentration (due to the relatively low absorption of alcohol into almost all other tissue, and in particular bone and fatty tissue), r cannot have a value of unity.

The spread of points on the graph (Figure I) indicates that there is no strict proportionality between the weight of an individual and the amount of alcohol necessary to reach a particular concentration in the blood, although a linear relationship is implied in the recent publication "Recognition of Intoxication" (British Medical Association, 1958). All other factors being equal, these two variables should be related, but there are clearly other physiological factors obscuring a simple mathematical relationship.

The results indicate that the weight factor begins to predominate over the other factors at the extreme ends of the weight range but, even then, there is only a general trend, and there are many deviations from a strict relationship. Consequently, in the interpretation of a blood alcohol concentration, it is considered that no allowance may justifiably be made for weight in the medium weight range (say 10 to 13 stone) other than that already included in the interpreting figure of 0·015%.

However, if this interpreting factor were applied to a person of considerably less than medium weight, it might be possible to overstate slightly the minimum consumption of alcohol, just as it is possible to understate grossly the figure in a heavy man. This point is well illustrated by reference to subjects 3 and 27 in Table I. For a concentration of, say, 0·225% in both subjects, the minimum consumption would be calculated as 15 glasses of beer. However, using the appropriate E_{max} values for each subject, they would in fact require 13·5 and 25·3 glasses respectively; even then, of course, the first figure would be overstated only if the rigid drinking conditions of the above-mentioned experiments were observed and if 0·225% was the maximum concentration reached. Nevertheless, it is because of this possibility that the interpreting figure is referred only to a man of medium weight and build.

Apart from the above-mentioned experiments, a number of other subjects was tested under similar conditions, except that the drinking was more prolonged and the rate of drinking, although always quite rapid, was not the fastest possible rate for each subject. E_{max} values have not been listed for these subjects, since this term is applied only where the drinking rate is at a maximum for the individual. Nevertheless, it was found that the concentration of alcohol added to the blood for the consumption of each seven-ounce glass of beer was always within the range 0·008% to 0·012%. This is in good agreement with the figures quoted above.

Summary.

The use and value of the blood alcohol test in evidence in charges of "driving under the influence" and related offences are discussed. The maximum concentration of alcohol added to the blood has been recorded in 54 different subjects after drinking beer (5%) at their maximum rate on an empty stomach: E_{max} values, representing the rise in blood alcohol concentration for each seven-ounce glass of beer taken, were then derived from these figures. The E_{max} values ranged from 0·0081% to 0·0167%, and a number of other experiments using less stringent drinking conditions gave comparable results. From these results, a blood alcohol concentration is interpreted in terms of the least amount of liquor which would normally be required to reach the particular concentration. The weight of an individual and the amount of alcohol necessary to reach a given concentration in the blood are not strictly proportional.

Acknowledgements.

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References.

BRITISH MEDICAL ASSOCIATION (1958), "Recognition of Intoxication", Report of a Special Committee of the British Medical Association.

GLAISTER, J. (1950), "Medical Jurisprudence and Toxicology", 9th Edition, E. & S. Livingstone Ltd., Edinburgh: 632.

GLAISTER, J. (1957), "Medical Jurisprudence and Toxicology", 10th Edition, E. & S. Livingstone Ltd., Edinburgh: 604, 606.

HANSMAN, F. S. (1953), "Driving under the Influence of Intoxicating Drink", MED. J. AUST., 2: 388.

JETTER, W. W. (1938), "Studies in Alcohol—1: The Diagnosis of Acute Alcoholic Intoxication by a Correlation of Clinical and Chemical Findings", *Amer. J. med. Sci.*, 196: 475.

KOZELKA, F. L., and HINE, C. H. (1941), "Method for Determination of Ethyl Alcohol for Medicolegal Purposes", *Industr. Engineering Chem. (Anal. Ed.)*, 13: 905.

NICKOLLS, L. C. (1956), "The Scientific Investigation of Crime", Butterworth, London: 333.

SMITH, S., and GLAISTER, J. (1939), "Recent Advances in Forensic Medicine", Churchill, London: 233.

VICTORIAN CRIMES ACT (1957), No. 6103, Section 408.

SOME ASPECTS OF ALCOHOL IN BODY FLUIDS. PART II. THE CHANGE IN BLOOD ALCOHOL CONCENTRATION FOLLOWING ALCOHOL CONSUMPTION.

By R. C. BAYLY

AND

N. E. W. MCCALLUM,

Laboratory of Forensic Science, Department of Pathology, University of Melbourne.

FOLLOWING the introduction of chemical tests of body fluids for their alcohol concentration as an aid in determining the condition of motorists suspected of driving while "under the influence of intoxicating liquor", certain problems have become evident in the application of the results obtained. One such arises since, in practice, there is always a lapse between the time a person comes under observation and the time a blood sample is taken. It has been found that this period may be as long as four hours. Since the concentration of alcohol in the blood of a person who has consumed alcohol will, at any particular time, depend on the relative rates of the processes of absorption from the intestinal tract and elimination from and destruction in the body, their combined action will result in a constantly changing blood alcohol concentration. It should be noted that, throughout the following discussion, the term "elimination" includes all the processes by which alcohol can be removed from the body.

It has been shown that alcohol is capable of rapid diffusion through the stomach wall (Bowden and McCallum, 1949). Hence, almost immediately after the drinking of alcohol, its absorption into the blood stream and distribution throughout the body begins. For medicolegal purposes, it is only the alcohol present in the tissues which is significant; unabsorbed alcohol still in the stomach or small intestine cannot exert any chemical influence on the individual at that particular time. For this reason, the rate of absorption of alcohol, which apparently differs from person to person, can be an important factor in charges relating to driving "under the influence" of alcohol.

As explained above, the relevant time in most cases is not the time at which the blood sample was taken, but rather some period before this. With the two factors of absorption and elimination differing in different people, the difficulty of assessing the alcohol concentration in the blood at some earlier time is apparent. In general, when a blood sample is taken, say, 75 minutes after a particular event, the concentration at the later time (t_2) may be related to the concentration at the earlier time (t_1) in one of three possible ways, as shown in Figure I.

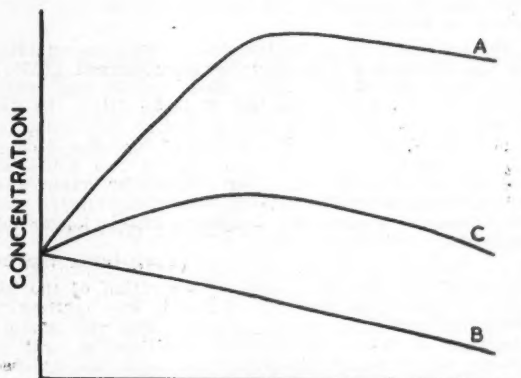

FIGURE I.

Graph of alcohol concentration against time for three individuals. The significance of the curves is explained in the text.

1. The alcohol concentration during this period may have risen (Curve A). Haggard and Greenberg (1934) calculated that absorption was not complete when the alcohol concentration was at its maximum in the blood. Hence, during this period of rising alcohol concentration, it is evident that the rate of absorption exceeds the rate of elimination from the blood. This rise would therefore suggest that at least part of the drinking was fairly recent.

2. The alcohol concentration may have fallen during the period (Curve B). There are two mechanisms whereby this could occur: (*a*) The concentration may have increased for a short time, passed through the zone of maximum concentration, and then fallen to a lower value at the end of the period. This also suggests that some of the drinking was fairly recent. (*b*) The concentration may have been at or past the maximum value, and a fall in concentration has occurred throughout the 75 minute period. These circumstances suggest that the period of drinking was more remote and that the process of elimination has predominated for at least 75 minutes before the blood sample was taken.

3. The alcohol concentration may be approximately the same at the time the sample was taken as it was 75 minutes previously (Curve C). The circumstances most likely to produce this phenomenon are that, during the

75-minute period, there was a period of rising concentration to reach the maximum, followed by a fall in concentration of similar magnitude to the previous rise.

While the existence of variation in the rates of absorption and elimination has been known for some time, relatively little information is available to assist in the assessment, from a known blood alcohol concentration, of the concentration at some previous time. The results of some investigations into changes occurring in blood alcohol concentration after drinking have been published. Jacobsen (1952), in a review of the metabolism of alcohol, concludes that, from the analysis of a blood sample for alcohol, it is not possible to predict accurately what the concentration may have been in a particular individual at some given time previous to the taking of the sample. Recently, Weinig and Schwerd (1955) investigated the rise in concentration in the blood after various conditions of drinking. They concluded that if all the circumstances of the drinking are known, it is possible to state, within certain limits, what the concentration may have been at some time prior to the taking of the blood sample. Gradwohl, in his text-book "Legal Medicine" (1954), states that "blood specimens should be taken at the earliest possible time, in order to minimize the amount of conjecture necessary in establishing the degree of intoxication at the time of arrest or accident".

In the report of a medical-legal committee established by the Australian Transport Advisory Council (1957), it was recommended that, if the blood sample was collected within one hour after the last alcoholic drink, the figure found by analysis should be accepted as the alcohol concentration of the blood at the time of the alleged offence. If the sample was taken from one to two hours after the end of drinking, the figure found by analysis was to be reduced at the rate of 0·016% per hour. Other provisions were made for samples taken at longer intervals after drinking.

In the present work, the aim was to investigate the extent of the rise in alcohol concentration of the blood after a period of drinking. Since it was realized that the most important factor affecting this rise would be the rate of alcohol absorption, conditions at first were chosen which would promote a maximum rate of absorption (see Part I); later, conditions were selected in an attempt to modify the absorption rate.

Experimental Studies.

In the tests, all subjects were males, ranging from near-teetotallers to heavy drinkers; many of the subjects are those used in the experiments described in Part I of this series and the subject's number is retained in this paper. An initial check was made on each subject for recently-consumed alcohol and, in the four cases in which this was detected (subjects 1, 7, 13 and 32), they were included in Experiment A when it was known that their blood alcohol concentration was on the decline. With the exception of the experiment in which the effect of food on the absorption of alcohol was studied, all subjects had taken only a light meal about three hours before drinking.

In the experiments using beer (5% alcohol v/v), the unit dispensed was a seven-ounce glass; when whisky (40% alcohol v/v) was used, the unit dispensed was seven eighths of an ounce diluted with an equal volume of water. The amount of alcohol in each of these units was therefore the same, although, in the experiments with whisky, there was a four-fold increase in the alcohol concentration of the beverage.

Immediately after the end of drinking, samples of blood and urine were obtained from the subjects, and further samples were obtained at intervals for at least two hours after drinking. These fluids were analysed by the method of Kozelka and Hine (1941).

The experiments now described were designed to determine the increase in blood alcohol concentration after a period of rapid drinking (Experiment A) and to study the changes produced in this rise by (i) altering the rate of drinking (Experiment B); (ii) altering the alcohol concentration of the beverage consumed (Experiment C) and (iii) the consumption of a substantial meal immediately before drinking (Experiment D).

The details of the experiments were as follows.

Experiment A.

A number of subjects drank beer at their fastest possible rate and, from the alcohol curve drawn for each subject, the following information was derived: (i) the concentration of alcohol (c_0) appearing in the blood at the cessation of drinking (expressed in grammes per 100 ml. of blood); (ii) the maximum alcohol concentration (c_{max}) reached in the blood; (iii) the rise in the concentration of alcohol ($c_{max} - c_0$) in the blood after the end of drinking; (iv) the time taken (t_{max}), expressed in minutes, to reach the maximum blood alcohol concentration.

TABLE I.

Results of Experiment A.

Subject.	A.	Drinking Time. (Minutes.)	c_0.	c_{max}.	Rise after Drinking. ($c_{max} - c_0$.)	t_{max}.
1	13	60	0·144	0·226	0·082	60
2	8	45	0·042	0·099	0·057	60
3	6	45	0·095	0·100	0·005	20
4	10·5	57	0·123	0·153	0·030	77
5	4	34	0·038	0·052	0·014	60
6	7	58	0·074	0·091	0·017	60
7	13	60	0·243	0·269	0·026	45
8	8	30	0·055	0·090	0·035	75
9	10	55	0·100	0·120	0·020	34
10	11	60	0·091	0·149	0·058	50
11	10	30	0·077	0·138	0·061	90
12	8	20	0·078	0·101	0·023	90
13	13	60	0·175	0·198	0·023	39
14	10·5	75	0·064	0·105	0·041	80
15	14	71	0·126	0·159	0·033	67
16	7	75	0·088	0·095	0·007	20
17	8	30	0·030	0·082	0·052	90
18	9	93	0·072	0·107	0·035	45
19	6	30	0·048	0·070	0·022	60
20	12	60	0·104	0·166	0·062	38
21	14	60	0·134	0·172	0·038	60
22	14	60	0·111	0·164	0·053	53
23	4	30	0·022	0·042	0·020	45
24	12	60	0·063	0·138	0·075	45
25	9	32	0·050	0·096	0·046	100
26	17	60	0·116	0·199	0·083	67
27	8	30	0·037	0·071	0·034	75
28	10	60	0·100	0·147	0·047	87
30	16	60	0·131	0·173	0·042	45
32	12	60	0·124	0·154	0·030	30
33	13	60	0·118	0·157	0·039	55
34	12	57	0·085	0·098	0·013	90
36	15	60	0·160	0·205	0·045	45
37	8	35	0·033	0·093	0·060	85
38	15	60	0·128	0·164	0·036	114
39	12	59	0·124	0·156	0·032	75
40	8	33	0·058	0·090	0·032	107
41	8	20	0·017	0·092	0·075	110
42	12	35	0·093	0·120	0·027	75
43	10	60	0·087	0·114	0·027	36
44	15	60	0·160	0·202	0·042	58
45	12	30	0·070	0·115	0·045	51
46	12	30	0·048	0·107	0·059	90
48	16	60	0·130	0·167	0·037	75
49	23	103	0·216	0·254	0·038	90
50	6	20	0·058	0·078	0·020	38
51	19	60	0·183	0·218	0·035	60
52	21	60	0·164	0·208	0·044	45
53	9	60	0·060	0·094	0·034	60
54	8	35	0·045	0·078	0·033	75
55	12	60	0·052	0·111	0·059	56
56	16	60	0·116	0·160	0·044	51
57	13	90	0·100	0·134	0·034	35
58	14·5	60	0·110	0·152	0·042	46
59	9	30	0·070	0·073	0·003	30
60	18	60	0·120	0·174	0·054	75

The results of this experiment are recorded in Table I, where A is the number of seven-ounce glasses of beer consumed. The time taken (in minutes) to consume this alcohol is also recorded.

Experiment B.

A group of the same subjects was used and the conditions of drinking were as follows. (*a*) Five units of beer were consumed at a regular rate in 50 minutes,

followed by ten units (evenly-spaced) in 50 minutes. (*b*) Ten units of beer were consumed at a regular rate in 50 minutes, followed by five units (evenly-spaced) in 50 minutes. In both cases, the total consumption was therefore 15 units of beer in 100 minutes.

Experiment C.

The beverage used was whisky, diluted to an alcohol concentration of 20%. In a preliminary experiment, four subjects drank 11 units of whisky in 55 minutes. Subsequently, six subjects drank 15 units of whisky at a regular rate in 60 minutes.

TABLE II.
Results of Experiment B.

Subject.	A.	Drinking Time. (Minutes.)	c_0.	c_{max}.	$(c_{max}-c_0)$.	t_{max}.
			(*a*) Rapid Rate of Drinking in Final Period.			
20	15	100	0·146	0·180	0·034	65
21	15	100	0·147	0·176	0·029	60
33	*15*	*100*	*0·130*	*0·168*	*0·038*	*62*
38	15	100	0·128	0·182	0·054	118
44	15	100	0·150	0·183	0·033	30
48	15	100	0·118	0·156	0·038	57
52	*15*	*100*	*0·148*	*0·163*	*0·015*	*40*
			(*b*) Rapid Rate of Drinking in Initial Period.			
20	15	100	0·137	0·168	0·031	36
21	15	100	0·181	0·196	0·015	36
33	15	100	0·162	0·187	0·025	42
38[1]						
44	15	100	0·162	0·172	0·010	38
48	15	100	0·133	0·164	0·031	88
52	15	100	0·151	0·167	0·016	32

[1] Results unavailable.

Experiment D.

The subjects were given a substantial meal of meat and vegetables prior to drinking, and biscuits and cheese were provided during the drinking period. Each subject consumed 15 units of beer under the same conditions as described in Experiment B (*a*).

The results of Experiments B, C and D are recorded in Tables II, III and IV respectively. In Table III, A is the number of units of whisky consumed by each subject.

TABLE III.
Results of Experiment C.

Subject.	A.	Drinking Time. (Minutes.)	c_0.	c_{max}.	$c_{max}-c_0$.	t_{max}.
21	11	55	0·128	0·133	0·005	25
22	11	55	0·092	0·126	0·034	36
33	11	55	0·080	0·107	0·027	38
44	11	55	0·118	0·124	0·006	24
20	15	60	0·135	0·174	0·039	45
21	15	60	0·140	0·197	0·057	36
22[1]	15	60	0·134	—	—	—
33	15	60	0·134	0·183	0·049	42
44	15	60	0·204	0·204	Nil	Nil
52	15	60	0·125	0·171	0·046	35

[1] Subject vomited 30 minutes after completion of drinking.

Discussion.

Under the conditions of drinking in Experiment A, it has been shown that a rise in blood alcohol concentration after the conclusion of drinking occurred in all of the 56 subjects tested. The magnitude of this rise ranged from 0·003% (subject 59) to 0·083% (subject 26), with an average value of 0·039%; the time taken for the subjects to reach their maximum concentration in the blood ranged from 20 minutes (subjects 3 and 16) to 114 minutes (subject 38) after the completion of drinking. There is no direct relation between this time (t_{max}) and either the amount of liquor consumed or the magnitude of the rise produced. It must again be emphasized here that these subjects drank at their maximum possible rate, which was, in many cases, exceptionally high.

It follows that the amount of alcohol consumed and the time during which it is consumed can limit the increase in concentration in the blood after drinking. Thus the results obtained from this experiment and in the previous work (Part I) show that it would not be possible for a concentration to rise, for example, by 0·08% after the drinking of only four seven-ounce glasses of beer. On the other hand, the consumption of, say, 14 glasses of beer would ordinarily require an appreciable time, so that, at the conclusion of drinking, a substantial amount of the alcohol would already be present in the blood stream.

TABLE IV.
Results of Experiment D.

Subject.	A.	Drinking Time. (Minutes.)	c_0.	c_{max}.	$c_{max}-c_0$.	t_{max}.
20	*15*	*100*	*0·132*	*0·152*	*0·020*	*55*
21	15	100	0·158	0·168	0·010	45
33	15	100	0·117	0·144	0·027	37
38	15	100	0·133	0·144	0·011	50
44	15	100	0·174	0·174	Nil	Nil
48	15	100	0·124	0·140	0·016	46
52	15	100	0·135	0·156	0·021	40

It would therefore be expected that, in general, the longer the time taken to drink a given amount of alcohol, the smaller will be the rise in the alcohol concentration after drinking is finished, although the rate of absorption will also be a factor in the effect observed. Clearly, the generalization is not always true since subject 59, who drank at two to three times the rate of subjects 3 and 16 and consumed a greater amount of alcohol, showed a rise of the same order as these.

TABLE V.
Results from All Subjects who Consumed 12 Units of Beer.

Subject.	A.	Drinking Time. (Minutes.)	Rise after Drinking.	t_{max}.
45	12	30	0·045	51
46	12	30	0·059	90
42	12	35	0·027	75
34	12	57	0·013	90
39	12	59	0·032	75
20	12	60	0·062	38
24	12	60	0·075	45
32	12	60	0·030	30
55	12	60	0·059	56

The converse, that the shorter the time taken to drink a given amount of alcohol, the greater will be the rise after drinking, is also not borne out by the results of these experiments. The following results (Table V) have been extracted from Table I. It will be seen that subject 46 drank alcohol at twice the rate of subject 55, but their rises after drinking are indentical, while the two highest rises are among those taking 60 minutes to consume the alcohol.

The effect of variation in the rate of drinking on the subsequent rise in the blood alcohol concentration was investigated in Experiment B, where, for comparative purposes, a group of the same subjects was used. The results in Table II show that the drinking rate can be a factor, as in three of the six subjects tested (subjects 21, 33 and 44), the rise in concentration ($c_{max}-c_0$) was significantly increased when the faster drinking rate

occurred in the last portion of drinking. However, although this is the effect which would be expected, it appears that variations in the rate of absorption can occur in one individual at different times, since in two of the subjects (44 and 48), a higher value of $c_{max} - c_0$ has occurred in a shorter time. Furthermore, a comparison of the results from subject 38 in Tables I and II shows that this subject gave a higher rise after drinking when he consumed the same amount of alcohol in a longer time.

A comparison of Tables I and III shows that the principal effect of increasing the alcohol concentration of the beverage was to reduce the time required for the alcohol to reach its maximum concentration in the blood. On the other hand, no clear-cut results emerge from comparisons of maximum concentrations attained after drinking equivalent amounts of beer or whisky; after drinking whisky, two subjects reached a higher concentration of alcohol than that produced by the equivalent amount of beer, while one reached a lower concentration and two were the same. Similarly, there was no uniform effect on the rise in concentration after drinking. In view of these variations, further work on this aspect was considered to be beyond the scope of this survey.

The action of food in the stomach in depressing the maximum concentration of alcohol reached in the blood after drinking was reported by Mellanby (1919), and, later, Eggleton (1940) concluded that certain constituents of foodstuffs could accelerate the metabolism of alcohol. The effect of food in the stomach on the rise in blood alcohol concentration after drinking is now shown by a comparison of Tables II(*a*) and IV. In all subjects there has been a decrease in the maximum blood alcohol concentration when food was present, while in six of the seven subjects, there was a reduced rise in concentration after drinking. Unexpectedly, six of the seven subjects attained their maximum concentration in a shorter time when drinking immediately after food; the time for the seventh subject was unchanged.

The rises observed in blood alcohol concentration after the completion of drinking are significant when related to the type of legislation which fixes an upper permissible concentration limit in the blood of motorists (see Part I). From the experiments, it is evident that an accurate assessment of the concentration of alcohol in the blood at some time before the taking of a blood sample is not possible. Even if the precise conditions of drinking are known, only an approximation can be given to the concentration at an earlier time, and it has to be borne in mind that the characteristics of the individual's absorption and elimination processes may predominate over these known drinking conditions. In general, the approximation will become less reliable as the taking of the blood sample is delayed. The possibility of the alcohol concentration changing during the period between the alleged offence and the time the sample was taken was apparently known to the New York legislators. This legislation, which gives *prima facie* effect to certain concentrations, provides that the relevant concentration is that found by analysis, but only if the blood sample is taken within two hours of the alleged offence.

Summary.

The rise in alcohol concentration in the blood after the completion of drinking was observed in 56 different male subjects who had consumed beer at their fastest rate on an empty stomach. This rise ranged from 0·003% to 0·083%, with an average value of 0·039%; in 14 of the subjects (25%), the rise exceeded 0·05%. When the drinking rate was varied, there was usually, but not always, a significant increase in this rise if the rapid period of drinking occurred in the final stages. The time taken for the attainment of the maximum blood alcohol concentration was reduced by increasing the concentration of the beverage, but no other clear-cut results were obtained from this. The presence of food in the stomach before drinking lowered the maximum concentration attained under otherwise indentical conditions, while in most subjects the rise in concentration after drinking and the time for attainment of the maximum concentration were reduced. It is concluded that an accurate assessment cannot be made of the blood alcohol concentration in an individual at some time prior to the taking of a blood sample.

Acknowledgements.

We wish to thank members of the Department of Pathology, University of Melbourne, for taking blood samples and assisting in the conduct of these experiments. In particular, we wish to acknowledge our debt to those several subjects who so willingly endured the exacting and sometimes harsh conditions of the experiments.

References.

AUSTRALIAN TRANSPORT ADVISORY COUNCIL (1957), "Voluntary Blood Tests for Assistance to the Courts in Determining Intoxication", Report of Medical-Legal Committee.

BOWDEN, K. M., and MCCALLUM, N. E. W. (1949), "Blood Alcohol Content: Some Aspects of its Post-Mortem Uses", MED. J. AUST., 2: 76.

EGGLETON, M. G. (1940), "Some Factors Affecting the Metabolic Rate of Alcohol", *J. Physiol.*, 98: 239.

GRADWOHL, R. B. H. (1954), "Legal Medicine", C. V. Mosby, St. Louis: 792.

HAGGARD, H. W., and GREENBERG, L. A. (1934), "Studies in Absorption, Distribution and Elimination of Ethyl Alcohol. III. Rate of Oxidation of Alcohol in the Body", *J. Pharmacol. exp. Ther.*, 52: 167.

JACOBSEN, E. (1952), "The Metabolism of Ethyl Alcohol", *Pharmacol. Rev.*, 4: 107.

KOZELKA, F. L., and HINE, C. H. (1941), "Method for Determination of Ethyl Alcohol for Medicolegal Purposes", *Industr. Engineering Chem. (Anal. Ed.)*, 13: 905.

MCCALLUM, N. E. W., and SCROGGIE, J. G. (1959), "Some Aspects of Alcohol in Body Fluids. Part I. Correlation between Blood Alcohol Concentration and Alcohol Consumption", MED. J. AUST., 2: 169.

MELLANBY, E. (1919), "Alcohol: Its Absorption into and Disappearance from the Blood under Different Conditions", Medical Research Council of the Privy Council, Special Report Series No. 31, H.M. Stationery Office, London.

WEINIG, E., and SCHWERD, W. (1955), *"Die Berechnung der Blutalkoholkonzentration zur Tatzeit und der Maximumbereich"*, *Dtsch. Z. ges. gerichtl. Med.*, 44: 55.

A SURVEY OF ALCOHOLISM.[1]

By IAN R. MACKAY,[2]

From the Clinical Research Unit of the Walter and Eliza Hall Institute of Medical Research and the Royal Melbourne Hospital, Melbourne.

> It is part of the deeper mystery and tragedy of life that whiffs and gleams of something that we immediately recognize as excellent should be vouchsafed to so many of us only in the fleeting earlier stages of what in its totality is so degrading a poison.—William James, "Varieties of Religious Experience".

IT can be estimated that there are over 100,000 victims of alcoholism in our country; these have become singled out from a total drinking population in Australia of about four to five million. The habit of drinking alcohol is widespread, and this is everywhere encouraged by persuasive advertisements that alcohol is a necessary adjunct to our social forgatherings and favourite recreations and even to our well-being.

There is no way of knowing precisely how many individuals suffer in health as a result of this popular social habit, for exact data on alcoholism are very difficult to obtain. A formula has been developed by Jellinek in the United States of America to estimate the number of sufferers from alcoholism in a given population (Keller,

[1] Based on a paper read at a meeting of the Section of Preventive Medicine of the Victorian Branch of the British Medical Association on March 12, 1959.

[2] Working with the aid of a grant from the National Health and Medical Research Council of Australia.

1958). This formula,[1] which is based mainly on reported deaths from cirrhosis of the liver, reads $A = \frac{PD}{K} \times r$, and may be applied to Australian data as follows. Of 100 subjects with cirrhosis studied in our Unit by Wood (1959), 51 were alcoholics—a figure for P of 0·51; this compares closely with the figure of 0·515 cited for the United States by Popham (1955). The total number of deaths from cirrhosis in Australia in 1952 was 408. The constant K has been derived from an international sample of chronic alcoholic subjects examined *post mortem*; the figure is smaller than might be expected. The ratio r is about 4·0 in the United States (Popham, 1955), and a similar figure is assumed for Australian conditions. It may thus be calculated that in 1952 there were some 120,000 alcoholics in Australia, or approximately 2000 per 100,000 persons aged over 20 years.

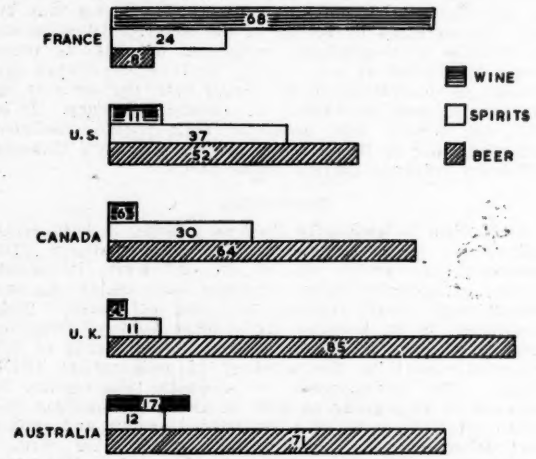

FIGURE I.

The proportions of alcohol consumed as wine, spirits and beer in France, the United States of America, Canada, the United Kingdom and Australia.

Whether or not the type of alcohol consumed has any bearing on the incidence of alcoholic disease is uncertain; however, it is a fact that the proportion of alcohol derived from wine, spirits and beer varies widely in different countries (Popham, 1955), as shown in Figure I.

Alcohol Consumption and Alcoholism—Australia and Abroad.

The extent of alcoholism and alcohol consumption in Australia and certain other countries is presented in Figure II. The incidence of alcoholism is presented as the rate per 100,000 persons aged over 20 years. The amount of alcohol consumed annually as gallons per person over 15 years ranges from 1·06 in Sweden to 2·95 in France. The figure for alcohol consumption in Australia of 2·07 gallons per person aged over 15 years is high; but, compared with other nations, Australia is favourably placed as regards the incidence of alcoholism (Figure II). Thus, although the alcohol habit in Australia is widespread and well indulged, there is a discrepancy between this high intake and the relatively low incidence of alcoholic complications; this may reflect the plentiful supply of foodstuffs and good nutritional status in this country.

Nevertheless, the rising trend of alcohol consumption in Australia over recent years and the contribution made by alcoholism to ill health in Australia present a serious problem. Beer consumption in Australia, which represents 70% of the nation's alcohol intake, has risen from 12·47 gallons per head in 1938-1939 to 24·74 gallons per head in 1955-1956; this trend, however, has slackened since 1954. Correspondingly, the beer production for Australia of a large brewery has risen from 40,000,000 gallons in 1951 to 58,000,000 gallons in 1958. The excise duty collected on beer alone reached the astonishing large sum of £A87,000,000 *per annum* in 1956. It is of interest that in 1952 the total liquor tax in France, with a far larger population and a greater consumption of alcohol, amounted to £A67,500,000 (Mouchot, 1955), whereas the Federal Government of Australia collected £A57,000,000 on beer alone in 1952, since when excise taxes have risen. The incomes to the Government from excise and to some breweries as net profits are of considerable magnitude and are rising. Surely the health authorities of the nation

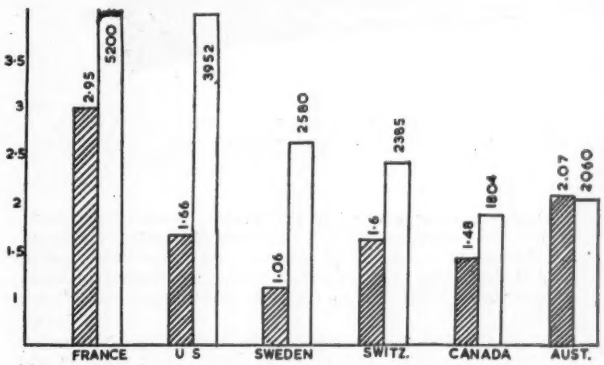

FIGURE II.

The incidence of alcoholism and annual per-capita alcohol consumption in the adult population in North America, Europe and Australia in 1952. From data cited by Popham (1955).

can claim liberal financial support for investigating this problem of alcoholism from its social and medical aspects!

Alcoholism in Public Hospital Patients in Victoria.

Alcoholism plays a significant role in determining illnesses leading to public hospital admission. A survey was made by Saint *et alii* (1952) of 222 medical in-patients in the Royal Melbourne Hospital on a given day; alcohol was found to be a direct cause of illness in 7·7%. More recently Professor J. G. Hayden (1959) evaluated all the patients in his unit at St. Vincent's Hospital over a six-month period. His figures indicated that alcohol was a direct cause of illness in 14% of all cases, and a contributing cause in 5%..

Social Factors in Alcoholism.

Social and occupational factors play an important role in establishing the alcohol habit, as shown by an analysis (Figure III) of the life saga of 52 consecutive patients whose alcoholism resulted in admission to our Unit (Wood, 1959). The habit of drinking heavily was established in early adult life in 75% of the cases; it was potentiated by occupational exposure in 34% of the cases and by a failure to establish normal family relationships in 44%. Later in life, a period of heavy drinking combined with malnutrition often corresponded with isolation precipitated by divorce, by marital separation, or by death of parents, so that in 40% of the 52 cases a solitary existence contributed to the urge to seek solace in alcohol.

[1] A = the total number of alcoholics with or without complications alive in a given year; P = the proportion of all deaths from cirrhosis attributable to alcoholism; D = the total deaths *per annum* from cirrhosis of the liver; K = the proportion of all chronic alcoholics who die of cirrhosis (a constant, 0·00693); and r = the ratio of all alcoholics to "chronic alcoholics".

The Pathology of Alcoholism.

The pathological effects of alcoholic malnutrition, as seen in public hospital populations, are shown in Table I. The figures are based on a survey of 78 alcoholics at the Royal Melbourne Hospital by Joske and Turner (1952), and of 56 consecutive alcoholic patients at St. Vincent's Hospital by Hayden (1959). These figures emphasize that the major impact of alcoholic malnutrition is upon the liver and nervous system.

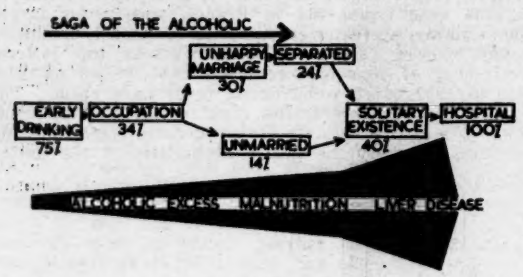

FIGURE III.

The life saga in 52 cases of alcoholism. Drinking in early adult life, occupational exposure and social isolation were important contributing factors.

Cirrhosis.

Alcoholic malnutrition is the major cause of cirrhosis of the liver in Australia; alcoholism accounted for 51 of an unselected series of 100 patients with cirrhosis studied in our Unit, and for more than twice the number of cases of cirrhosis (21) due to chronic viral hepatitis (Wood, 1959).

Alcoholic cirrhosis is preceded by a stage of fat accumulation in the liver—the so-called fatty liver; this is the result of an imbalance in fat-producing and fat-mobilizing factors in the diet. Lipogenic foodstuffs comprise fats and carbohydrates and include the calories provided by alcohol itself. Lipotropic or fat-mobilizing factors are available in protein foods; choline is an important lipotropic substance. Pancreatic insufficiency may be implicated in this type of nutritional defect (*vide infra*). General starvation does not produce a fatty liver, since the essential nutritional defect in the production of a fatty liver is a disproportion between the total calorie intake and the protein content of the diet. Kwashiorkor, the protein deficiency disease of the tropics, appears to have a similar pathogenesis to the nutritional cirrhosis of "civilized" communities.

TABLE I.

Basis of Symptoms in 78 Alcoholics (Royal Melbourne Hospital) and 56 Alcoholics (St. Vincent's Hospital, Melbourne, 1958).[1]

Pathological Basis.	Series.	
	Royal Melbourne Hospital.	St. Vincent's Hospital.
Nervous system:		
Peripheral neuritis	13 } 23 (30%)	9 } 12 (22%)
Encephalopathy	10 }	3 }
Liver:		
Nutritional hepatitis	20 } 22 (28%)	20 } 20 (36%)
Acute necrosis	2 }	0 }
Stomach:		
Gastritis	6 } 12 (15%)	0 } 9 (17%)
Peptic ulcer	6 }	9 }
Cardiac failure	3 (4%)	5 (9%)
Others	18	6
Total	78	56

[1] From data of Joske and Turner (1952) and Hayden (1959).

Hepatomegaly due to fatty liver is frequently detected in alcoholics at the end of a drinking bout, but under the influence of a good diet complete resolution may occur. Occasionally circumstances are less favourable. The nutritional insult to the liver may be prolonged, the circulation may be impaired with resultant anoxic damage to the liver, or infections such as pneumonia may intervene with resulting toxæmia. Then the fatty lesion is associated with cell necrosis, and the characteristic histological picture of nutritional liver disease develops. Eosinophilic strands, referred to as "alcoholic hyaline", are seen within damaged, necrotic and fat-laden liver cells. Cell necrosis is followed by fibrosis, and ultimately the typical cirrhotic liver is produced. Further episodes of liver damage may be followed by repair and regeneration, but ultimately a stage of hepatic decompensation is reached, manifested by jaundice, ascites or œsophageal varices. Death may result from liver failure or torrential bleeding from varices.

Neuropathy.

Alcoholism is associated with degenerative lesions in the nervous system, one component of which is a loss of the myelin sheath from nerve fibres. The lesion may be well demonstrated by biopsy of the anterior tibial nerve in patients with alcoholic peripheral neuritis, as illustrated by Finckh *et alii* (1952); in their experience the amount of demyelination paralleled both the severity of the neuritis and the history of dietetic deficiency. It is still not certain how alcoholic malnutrition mediates demyelination in the nervous system, although thiamin deficiency certainly plays a major part.

Pancreatitis.

Alcoholism is frequently cited as a factor in both acute and chronic relapsing pancreatitis. Of 43 patients with relapsing pancreatitis studied in our Unit, 10 drank alcohol excessively; these comprised nine males and one female, and their average age was 40 years. This experience is in keeping with other surveys, wherein alcoholism made a significant contribution (29% of 849 collected cases) to the ætiology of pancreatitis (Bell, 1958). The pathogenesis of alcoholic pancreatitis is believed to be similar to that of alcoholic hepatitis, the lesion being the result of a conditioned protein and amino-acid deficiency; the experimental production of chronic pancreatitis with the methionine antagonist, ethionine, supports this concept (Popper *et alii*, 1954).

Woldman *et alii* (1959) have stressed the important role of alcoholism in pancreatic disease, and have suggested that both the fatty liver and nutritional cirrhosis were determined primarily by pancreatic insufficiency. The familiar persistence of a large fatty liver in the reformed alcoholic is best explained on this hypothesis, particularly if there have been antecedent attacks of pancreatitis.

Heart Disease.

A small proportion of chronic alcoholics will present with cardiac failure, which probably represents wet beriberi. Since the response to thiamin is occasionally not dramatic, there is a tendency to implicate other dietary deficiencies or a direct toxic effect of alcohol on the myocardium, and to refer to the heart failure of the alcoholic as "nutritional" or "alcoholic" myocarditis. Eliaser and Giansiracusa (1956) described "alcoholic myocardosis" unrelated to vitamin deficiency or liver disease, and also "nutritional heart disease", as well as the classical beriberi heart disease of chronic alcoholism. Frederiksen and Hed (1958) demonstrated electrocardiographic abnormalities in 19 out of 121 male chronic alcoholics, and attributed the cardiac lesions to chronic alcoholism in these cases.

Alcohol and Traffic Fatalities.

Possibly the greatest hazard of all for the drinker (and all in his environment) is injury and violent accidental death. In this context, I shall consider traffic accidents alone, although intoxication contributes to other accidental deaths as well (Bowden *et alii*, 1958).

In Victoria, three series of traffic accident victims have been investigated by blood alcohol tests. The figures cited in series A and B are those of Birrell (1959). In series A, tests were performed on 100 consecutive accident victims

brought to the casualty department of a metropolitan hospital; a positive result to a blood alcohol test was obtained in 76% of all victims, and in 56% of motor-car drivers. It is, of course, impossible to predict what proportion of all car drivers and pedestrians would give a positive result to a blood alcohol test in the period from 4 p.m. to 10 p.m. when accidents are most common. In series B, 173 serious road accidents were investigated by a police accident squad; there were 125 deaths, and in 65 of these deaths alcohol was implicated. Series C, compiled by Bowden *et alii* (1958), refers to blood alcohol tests on traffic accident victims brought to a city morgue. Although some selection of cases had been made, it was shown that at least 25% of all the motor-car drivers killed had a blood alcohol content of 0·1% or more; Birrell (1959) has estimated that up to 50% of all traffic accident victims tested at the morgue would give a positive response to a blood alcohol test. Moreover, Pearson (1957)

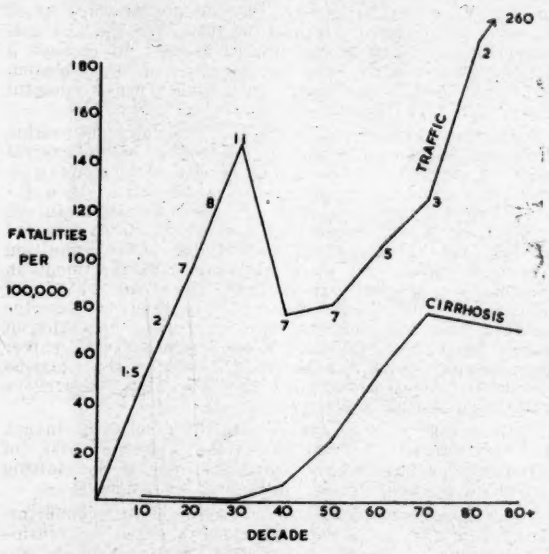

FIGURE IV.

Deaths per 100,000 persons from traffic accidents and cirrhosis of the liver in Australia in 1955, plotted by decades of life. The male-female sex ratio is shown alongside the traffic graph; alcohol may be particularly implicated in the peak involving males in the 20 to 30 years group.

in Western Australia found blood alcohol levels greater than 0·1% in 39·4% of 218 consecutive unselected traffic accident victoms who survived for less than 12 hours after the accident; of these victims, 34% of the motorists and 45% of the pedestrians had blood alcohol levels over 0·1%.

In Figure IV are plotted the deaths per 100,000 population from traffic accidents and cirrhosis of the liver in 1955 in Australia by decades of life. Deaths from cirrhosis rose in middle age, and the graph reached a plateau in the seventh decade. Deaths from traffic accidents rose to a peak in the third decade, with a striking preponderance of males over females (11 to 1) for the years 25 to 30; the curve then fell, and rose steeply again in old age, illustrating the vulnerability of the aged to road hazards. Since the alcohol habit begins in early adult life and has a high incidence in males, particular attention should be paid to the traffic accident peak involving males in the 20 to 30 years decade, wherein alcohol may play a particularly significant role.

There were 2219 persons killed in motor vehicle accidents in Australia in 1956, whereas deaths from alcoholic cirrhosis would number 200 to 300. Hence, if it is accepted that alcohol may be involved in 30% to 40% of our 2000 odd annual fatalities from traffic accidents, the heavy drinker appears to run a greater hazard of dying in a road accident than from cirrhosis or other medical effects of alcoholic malnutrition.

Conclusions.

The health hazard of alcoholic malnutrition and alcohol-induced accidents ranks high on the list of problems to be faced in the field of preventive medicine, and considerably more knowledge is required concerning the medico-social factors related to alcoholism which operate in our community. The scope of inquiry should embrace genetic and constitutional factors, home environment, intelligence, social rank and psycho-social adjustments, as well as the incidence of tissue lesions. Alcoholism should be regarded in its true light as an endemic disease, responsible for high rates of morbidity and costly utilization of our medical facilities. Since this approach would require the combined resources of medicine, psychiatry and sociology, we must visualize alcohol clinics, with in-patient and out-patient facilities, well staffed with highly trained clinicians, psychiatrists, biochemists and social workers. Such a clinic should not necessarily depend upon pre-existing agencies for its establishment or support. The evidence presented in this paper alone demands a vigorous approach to the whole question of alcoholism in Australia, so that we may know far more than we now do about its causation and background. There is a call for wide-scale medico-social research into this pressing and increasing problem.

Summary.

There is a rising trend of alcohol consumption *per capita* in Australia.

Patients with illnesses attributable to alcoholism comprise a considerable proportion of those admitted to public hospitals.

Diseases resulting from alcoholic malnutrition include cirrhosis of the liver, encephalopathy and neuropathy, cardiac failure, pancreatitis and gastritis.

Alcoholic intoxication contributes significantly to the 2000 or more fatalities from traffic accidents *per annum* in Australia. Males in the 20 to 30 years decade of life may represent a special risk.

Alcoholism results in a costly utilization of our medical facilities. It is a medico-social problem in this country which demands wide-scale investigation.

Acknowledgements.

I am indebted to Professor J. G. Hayden and Dr. J. H. W. Birrell for permission to cite certain of their findings. Data were also obtained through the courtesy of the medical staff of the Royal Melbourne Hospital.

References.[1]

BELL, E. T. (1958), "Pancreatitis", *Surgery*, 43: 527.

BIRRELL, J. H. W. (1959), personal communication.

BOWDEN, K. M., WILSON, D. W., and TURNER, L. K. (1958), "A Survey of Blood Alcohol Testing in Victoria (1951 to 1956)", MED. J. AUST., 2: 13.

ELIASER, M., jr., and GIANSIRACUSA, F. J. (1956), "The Heart and Alcohol", *Calif. Med.*, 84: 234.

FINCKH, E. S., DALS, B. G., JOSKE, R. A., and SAINT, E. G. (1952), "Studies in Chronic Alcoholism. III. Laboratory Studies", MED. J. AUST., 2: 738.

FREDERIKSEN, P., and HED, R. (1958), "Clinical Studies in Chronic Alcoholism. III. Cardiac Changes in Chronic Alcoholism: An Electrocardiographic Study", *Acta. med. scand.*, 162: 203.

HAYDEN, J. G. (1959), personal communication.

JOSKE, R. A., and TURNER, C. N. (1952), "Studies in Chronic Alcoholism. I. The Clinical Findings in 78 Cases of Chronic Alcoholism", MED. J. AUST., 2: 729.

KELLER, M. (1958), "Alcoholism: Nature and Extent of the Problem", *Ann. Amer. Acad. polit., soc. Sci.*, 315: 1.

MOUCHOT, G. (1955), "Letter from France", *Int. J. Alcohol*, 1: 75.

[1] Certain of the statistical data were obtained from the office of the Commonwealth Statistician, Melbourne, and from the Year Books of the Commonwealth of Australia, Numbers 41 to 44, edited by the Commonwealth Bureau of Census and Statistics, 1955-1958.

PEARSON, A. T. (1957), "Alcohol and Fatal Traffic Accidents", MED. J. AUST., 2:166.

POPHAM, R. E. (1955), "A Statistical Report Relating to Alcoholism and the Use of Alcoholic Beverages in Canada", *Int. J. Alcohol*, 1:5.

POPPER, H., DE LA HUERGA, J., and KOCH-WESER, D. (1954), "Hepatic Injury Due to Conditioned Sulfo-Amino Acid Deficiency", *Ann. N. Y. Acad. Sci.*, 57:936.

SAINT, E. G., JOSKE, R. A., MACKAY, M. A. and TURNER, C. N. (1952), "Studies in Chronic Alcoholism. IV. Treatment and Management", MED. J. AUST., 2:743.

WOLDMAN, E. E., FISHMAN, D., and SEGAL, A. J. (1959), "Relation of Fibrosis of the Pancreas to Fatty Liver and/or Cirrhosis. An Analysis of 1,000 Consecutive Autopsies", *J. Amer. med. Ass.*, 169:1281.

WOOD, I. J. (1959), "Chronic Nutritional Disease of the Liver and Pancreas. An Australian Study", "Proceedings of the World Congress of Gastroenterology", in the press.

WORLD HEALTH ORGANIZATION (1958), "Annual Epidemiological and Vital Statistics, 1955".

ACQUIRED HYPOFIBRINOGENÆMIA IN PREGNANCY.

By N. A. BEISCHER,

Royal Women's Hospital, Melbourne.

THIS paper reviews the management of 20 patients with hypofibrinogenæmia at the Royal Women's Hospital, Melbourne, from January, 1956, until June, 1958.

Acquired hypofibrinogenæmia is a condition in which the plasma fibrinogen level falls below normal. An accepted normal level of fibrinogen is 220 to 400 mg. per 100 ml. of plasma, although different workers have reported various normal levels in pregnancy (Hodgkinson *et alii*, 1955). During normal pregnancy, plasma fibrinogen levels are increased above normal non-pregnant levels, and during labour may reach 600 mg. per 100 ml. of plasma (Barry *et alii*, 1955). The critical level of plasma fibrinogen, below which hæmorrhage of incoagulable blood may occur, has been variously estimated as between 150 and 200 mg. per 100 ml. of plasma (Hodgkinson *et alii*, 1955).

The overwhelming majority of transient blood coagulation defects complicating pregnancy and the puerperium are due to acquired hypofibrinogenæmia (Barry *et alii*, 1955). Even in acute leukæmia, in which fibrinogen is not the only factor in the clotting mechanism which may be inadequate, post-partum hæmorrhage of incoagulable blood was controlled by fibrinogen therapy in the two cases so far reported (Yahia *et alii*, 1958).

At the Royal Women's Hospital, Melbourne, commencing in December, 1955, the clot observation test described by Weiner *et alii* (1950) has been adopted as the criterion for the diagnosis of critical hypofibrinogenæmia. This test is performed by the withdawal of approximately 5 ml. of blood, usually from the brachial vein, and it is allowed to stand, uncitrated, in a test tube. The blood is then observed at regular intervals during the following hour. This clot observation test is performed immediately after the admission to hospital of all patients with ante-partum hæmorrhage or with known fœtal death *in utero*. Critical hypofibrinogenæmia is diagnosed if a normal clot fails to form within 20 minutes, or if a clot forms and subsequently dissolves.

The clot dissolution seen in some patients with hypofibrinogenæmia (six patients in this series) is due either to relative fibrinopenia, with consequent formation of a friable readily-dissolved blood clot, or to an increased level of circulating fibrinolysins. Drevermann has emphasized that the clinical evidence indicates that increased fibrinolytic activity of the plasma plays a major role in the development of hypofibrinogenæmia. This viewpoint could explain why some patients require massive doses of fibrinogen to restore their clotting mechanism to normal.

The clotting test provides the following clinical data (Barry *et alii*, 1955): (i) a stable clot indicates that the plasma fibrinogen level exceeds 150 mg. per 100 ml.; (ii) partial clot dissolution indicates a fibrinogen level of between 100 and 150 mg. per 100 ml.; (iii) a fragile, rapidly-dissolved clot indicates a level of 60 to 100 mg. per 100 ml.; (iv) absence of clot formation indicates a fibrinogen level below 60 mg. per 100 ml. All patients in groups (ii), (iii) and (iv) have critical hypofibrinogenæmia, and irrespective of the degree of fibrinopenia, are treated with the same routine specific fibrinogen therapy.

Routine biochemical estimation of plasma fibrinogen, although previously performed, has been replaced by the above-mentioned clot observation test as a diagnostic procedure since (i) biochemical estimations take several hours to perform and are often inaccurate; (ii) the clot observation test is rapidly and easily performed clinically, and may be repeated when indicated, as a therapeutic and diagnostic index.

A possible disadvantage of reliance on the clot observation test alone is that the clotting time may remain within normal limits, when a degree of fibrinopenia exists of such magnitude that surgical manipulation is hazardous to the patient (Barry *et alii*, 1955). However, more accurate biochemical investigations are unlikely to forewarn us of this rare predicament, as the time taken for the test precludes its assistance in the clinical assessment of such a patient. The recently described methods of rapid plasma fibrinogen estimation may ultimately prove helpful (Schneider, 1952).

From the viewpoint of treatment, the value of routine fibrinogen estimations, for the detection of subcritical states of fibrinogen depletion in cases of patients with known predisposing conditions, seems doubtful since (i) some authors have reported hypofibrinogenæmia in all cases of accidental hæmorrhage which were investigated (Hodgkinson *et alii*, 1955), yet clinically the condition became manifest, and therefore worthy of treatment in less than 5% of such patients (Sawitsky *et alii*, 1955); (ii) some patients in whom there is prolonged intrauterine retention of a dead fœtus do show progressive depletion of plasma fibrinogen, but most of such patients will deliver spontaneously and uneventfully before the plasma fibrinogen reaches the critical level at which hæmorrhage of incoagulable blood may occur.

With specific therapy available in the form of fibrinogen for intravenous administration, the maternal risk of uncontrollable hæmorrhage seems minimal, if the clotting test alone is employed as a means of assessment.

There has been no maternal death due to hypofibrinogenæmia at the Royal Women's Hospital since the routine management of hypofibrinogenæmia outlined above was adopted in December, 1955, and all of the 20 patients with this condition diagnosed since then have been delivered vaginally.

Critical hypofibrinogenæmia, although an obstetrical emergency, is not as dangerous to the mother as has been reported, and it is doubtful whether Cæsarean section, hysterotomy and especially hysterectomy, all of which have their advocates, are even indicated (Stouffer *et alii*, 1958; Pritchard and Ratnoff, 1955; Schneider, 1954).

Incidence.

One patient per 1400 booked admissions developed critical hypofibrinogenæmia during the thirty-months' period reviewed. This is a lower incidence than the one per 1000 admissions reported by Klein *et alii* (1956). In this period there were 225 booked patients treated for accidental hæmorrhage, an incidence as quoted by Townsend (1957) of 1·1% and eight of these patients developed critical hypofibrinogenæmia.

Thus approximately 3·5% of patients with accidental hæmorrhage developed hypofibrinogenæmia. Sawitsky and Plotkin (1955) have reported an incidence of 5% in cases of accidental hæmorrhage.

Also accidental hæmorrhage was the predisposing condition in 13 of the 20 cases diagnosed, that is, in 65% of the patients in this series.

Ante-Natal Supervision.

Nine patients had had completely uneventful ante-natal records prior to the onset of symptoms which resulted in their admission to hospital.

Four patients had prolonged retention of a dead fœtus. Two were rhesus isoimmunized, but in the other two there was no demonstrable cause of the fœtal death *in utero*.

Three patients had shown signs of preeclampsia sufficient to warrant their admission to hospital during pregnancy.

Two patients had essential hypertension, the diagnostic criterion being two or more blood pressure recordings above 140/90 mm. of mercury in the first trimester.

One patient had labile hypertension, which was treated throughout pregnancy with "Serpasil". This diagnosis was based upon the patient's frequently elevated systolic blood pressure, without an increased diastolic pressure, the former subsiding when the patient was rested.

One of the non-booked patients had no available ante-natal records.

Modes of Presentation.

Accidental Hæmorrhage.

Ten cases presented with severe abdominal pains and vaginal bleeding and were diagnosed on the patient's admission to hospital as accidental hæmorrhages. Three of these patients stated that fœtal movements had ceased since the onset of uterine pain.

All of these patients on admission to hospital showed absence of a normal clotting mechanism by means of the clot observation test, and were thus diagnosed as having critical hypofibrinogenæmia. It appears that fibrinogen depletion rapidly follows the accidental hæmorrhage, since most of these cases were diagnosed within two hours of the onset of abdominal pain.

Vaginal hæmorrhage on admission to hospital was not severe in four of these patients, and thus routine clot observation tests in all cases of ante-partum hæmorrhage allows early diagnosis of hypofibrinogenæmia; diagnosis may otherwise be delayed until severe post-partum hæmorrhage occurs.

Plasma fibrinogen estimations performed in six of these patients revealed levels of from 15 to 140 mg. per 100 ml., prior to treatment.

One of these patients at delivery was found to have a type II placenta prævia, which was encountered when rupture of the membranes was performed. There was, however, a ten-ounce old retroplacental clot also present, and in view of this and the history of abdominal pain, this case was regarded as one of accidental hæmorrhage. Placenta prævia has yet to be implicated as a predisposing cause of critical hypofibrinogenæmia.

Undiagnosed Ante-Partum Hæmorrhage.

Two cases presented with vaginal bleeding alone; one was provisionally diagnosed as mild accidental hæmorrhage, and the other as placenta prævia. Critical hypofibrinogenæmia was diagnosed in both cases by means of the clot observation test. Both patients eventually delivered placentæ showing retroplacental hæmatomata, and hence the diagnosis of accidental hæmorrhages was finally made.

One patient was an overdue preeclamptic in whom labour was induced by medical stimulation, with resultant ante-partum loss of incoagulable blood.

Prolonged Fœtal Death in Utero.

Four patients in this series had prolonged intrauterine retention of a dead fœtus, the fœtus having died six weeks prior to delivery in two cases, and seven and eleven weeks prior to delivery in the others. These patients confirm previous reports that fibrinogen depletion does not reach critical levels in this syndrome until the fœtus has been dead for at least five weeks.

In two of these cases fœtal death was presumed due to rhesus isoimmunization, one patient having had a previous hydropic infant, the other having had two previous infants requiring exchange transfusion. Fœtal maceration in both precluded microscopic confirmation of erythroblastosis.

On admission, two patients with fœtal death *in utero* exhibited spontaneous bruising, and yet one of them, who had a plasma fibrinogen level of 56 mg. per 100 ml. and a positive result to the clot test, was delivered, after medical induction of labour, without the occurrence of post-partum hæmorrhage. The absence of hæmorrhage in this case, without either fibrinogen or blood transfusion having been given, suggests that the well-contracted myometrium has a major role in effecting hæmostasis at the site of placental implantation (Barnes, 1947).

Thrombosis of placental vessels prior to delivery is another possible explanation of the absence of hæmorrhage in such cases.

The second patient with spontaneous bruising, and who paradoxically had a normal result to the clotting test prior to the induction of labour by an intravenous infusion of "Pitocin", developed severe ante-partum and post-partum hæmorrhage.

It is now considered hazardous to use oxytocics in such cases unless the clotting mechanism is previously restored by fibrinogen given intravenously. Such a case belongs to the small group in which treatment can be directed by a serum fibrinogen estimation, which shows the amount of fibrinogen necessary to raise the circulating level to normal.

The management of fœtal death *in utero*, because of the risk of hypofibrinogenæmia developing, poses the problem of whether or not labour should be induced. Several authors advocate weekly plasma fibrinogen estimations in these cases, and perform hysterotomy should fibrinogen depletion be detected. Others believe that induction by rupture of the membranes, with or without "Pitocin" administration, is indicated.

It is current policy at the Royal Women's Hospital to allow such patients to enter labour spontaneously, since most will be delivered before critical hypofibrinogenæmia develops, and the patients are advised to report promptly any vaginal hæmorrhage or the occurrence of spontaneous bruising. Spontaneous bleeding usually is vaginal, or into the skin, although epistaxis and alimentary hæmorrhage do occur. Fortunately, cerebral hæmorrhage does not seem to be a risk in these cases.

Post-Partum Hæmorrhage.

Two cases were diagnosed by the clotting test when extensive post-partum hæmorrhage followed normal deliveries.

One patient presented when post-partum hæmorrhage followed a delivery induced by artificial rupture of the membranes, the indication being labile hypertension at term.

Hypofibrinogenæmia is not widely recognized as a possible cause of post-partum hæmorrhage following uneventful deliveries, although Hopkins has reported three such cases, which occurred in his own general practice.

Mode of Delivery and Manipulative Interference.

All 20 patients were delivered vaginally, and apart from one outlet forceps and one breech extraction (the patient with placenta prævia), the deliveries were spontaneous.

Six patients required manual removal of the placenta, the indication in each instance being extensive post-partum hæmorrhage. Three of these patients had accidental hæmorrhages; two were patients in whom labour had been normal until completion of the second stage, and the other had prolonged fœtal death *in utero*, and this patient had an unusually fibrotic and adherent placenta, which was removed with difficulty.

After manual removal of the placenta, the uterus was packed in two cases as hæmorrhage continued. This procedure is seldom employed at the Royal Women's Hospital, and in neither of the patients did it control the hæmorrhage until fibrinogen was given intravenously.

Two patients had manual exploration of the uterus performed, when severe post-partum hæmorrhage followed delivery of the placenta. The uterus was atonic in one of

these cases, but in the other it was firmly contracted in spite of the extensive hæmorrhage. In neither case were placental remnants found, and both patients were severely collapsed after manual exploration.

Adequate resuscitation by blood transfusion and recognition and correction of a defective clotting mechanism should therefore precede manual exploration, as hypofibrinogenæmia and not retained placental elements may be the cause of the post-partum hæmorrhage.

Artificial rupture of the membranes was performed in three cases of patients with accidental hæmorrhage, who failed to come into labour spontaneously, and this procedure was done as soon as the clotting mechanism had been corrected, and did not initiate further hæmorrhage, irrespective of the state of dilatation of the cervix.

Uneventful deliveries occurred in these cases in which labour was induced by rupture of the membranes, and thus hypofibrinogenæmia does not constitute a maternal indication for Cæsarean section in accidental hæmorrhage (Townsend, 1957).

In this series there was only one patient with impaired renal function, and she was admitted as an emergency, presenting with accidental hæmorrhage and anuria. This patient regained normal renal function after a prolonged convalescence, and her anuria was probably related to the lack of early replacement of blood loss, and not to hypofibrinogenæmia, the latter developing two hours after her admission to hospital.

Perinatal Mortality.

The stillbirth rate was 75% (15 of the 20 infants). One infant died from pneumonia four hours after delivery, and another died due to prematurity and hyaline membrane six hours after delivery. The perinatal mortality was thus 85% in this series.

The three infants who survived were those of the three patients who presented when post-partum hæmorrhage followed normal deliveries, and therefore in this series the fœtal mortality was 100%, if hypofibrinogenæmia became clinically manifest with the fœtus still *in utero*. Boyd (1958) has suggested that some of these infants may succumb *in utero* from hypofibrinogenæmia in the baby. Fibrinolysins or thromboplastins may enter the fœtal circulation direct, at the site of the accidental hæmorrhage or by way of the maternal circulation, and cause defibrination of fœtal blood, with consequent pulmonary hæmorrhage into the fœtal lungs. It is also possible that this mechanism could cause fœtal death in cases of accidental hæmorrhage in which critical hypofibrinogenæmia never develops.

The average period of gestation at delivery (Figure I) was 34 weeks in this series, and thus prematurity is another possible factor in the poor fœtal salvage.

The average age of patients was 32 years (Figure II) and the average parity was three (Figure III).

Amount of Intravenous Fibrinogen Administered.

The average total amount of fibrinogen given intravenously in this series was 10·2 grammes, and varied from none at all to 28 grammes. Each gramme of fibrinogen was dissolved in 50 ml. of normal saline, this solution forming much more rapidly than when distilled water was used. The presence of pre-eclampsia does not contraindicate the use of saline as a solvent for the fibrinogen (Drevermann).

At the Royal Women's Hospital the present routine is to give an initial dose of 8 grammes of fibrinogen intravenously, and this high dose is given in the belief that a certain amount will be destroyed by circulating fibrinolysins. With this dose the clotting time in most cases was restored to normal, and further administration of fibrinogen seldom proved necessary.

Many of the recent papers give scant attention to fibrinogen therapy, and the various doses tend to be much lower than those stated above. However, when it is recalled that the total normal fibrinogen content of the circulating plasma is 8 to 12 grammes (Barnett and Cussen, 1954), it seems logical to favour these large doses, for the fibrinogen level must fall at least 60% before the clotting mechanism fails.

McBride (1958) suggests an initial dose of 4 grammes of fibrinogen to restore the critical fibrinogen level, whereas the above-mentioned dosage aims at restoration of the normal circulating level, which is approximately double the critical level.

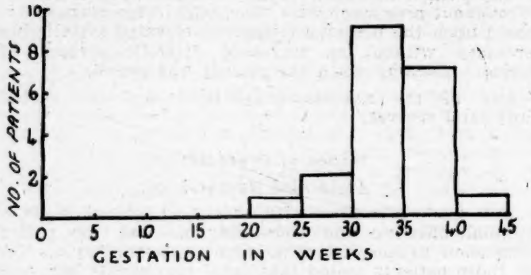

FIGURE I.

The risk of homologous serum jaundice following fibrinogen therapy has led McBride (1958) to suggest that fibrinogen dosage should be restricted where possible, and others have abandoned its use on these grounds. This fear

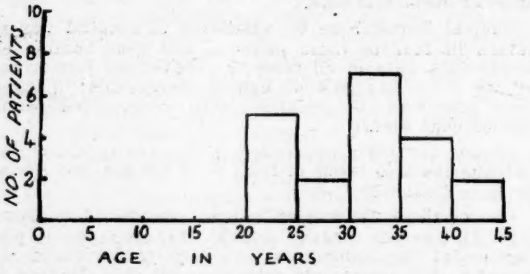

FIGURE II.

seems out of proportion, as hypofibrinogenæmia is a true obstetrical emergency, specifically controlled by fibrinogen therapy, and is a significant factor in maternal deaths from hæmorrhage (Lewis, 1956). None of the patients in

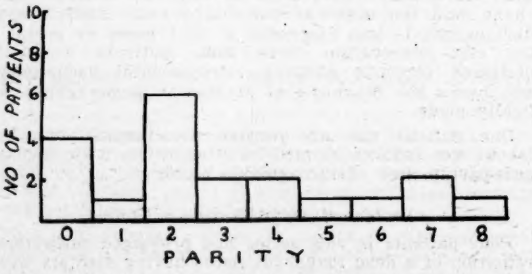

FIGURE III.

this series developed jaundice after fibrinogen treatment, and it seems that the risk of this complication should not influence treatment.

Two patients were momentarily shocked after the intravenous administration of fibrinogen, and the explanation of this is uncertain. The effect seemed too temporary to be attributed to intravascular coagulation resulting in

fibrin embolic phenomena. There were no signs of pulmonary collapse in these cases which demonstrated the "fibrinogen shock" syndrome.

Amount of Blood Transfused.

The average amount of blood transfused was 7·5 pints, and varied from none at all in one patient to 15 pints in another.

Even with early diagnosis and prompt fibrinogen treatment, blood transfusion is almost always necessary, the patient being shocked, either from frank blood loss or by the associated accidental hæmorrhage.

Blood transfused should, when possible, be fresh, as stored blood has a plasma fibrinogen level of approximately only 165 mg. per 100 ml. Also, the inhibitor level of fresh blood appears to be greater than that of stored blood, and this may be of value in the control of the fibrinolytic enzyme system (Yahia *et alii*, 1958).

Conclusions.

1. Accidental hæmorrhage is the commonest predisposing condition in the development of hypofibrinogenæmia.

2. Critical hypofibrinogenæmia may develop after normal deliveries, hence the importance for routine clotting tests to be performed in all cases of moderate or severe post-partum hæmorrhage. This may particularly apply when labour has been induced by the use of oxytocic drugs.

3. Fibrinogen and blood transfusion therapy must be instituted as soon as diagnosis permits, and the initial suggested fibrinogen dosage is 8 grammes.

Acknowledgements.

I am grateful to Professor Lance Townsend for his suggestions and advice in the writing of this paper. I also wish to thank the members of the honorary medical staff of the Royal Women's Hospital, Melbourne, for permission to examine the histories of the patients who were under their care.

References.

BARNES, A. C. (1947), "Post-Partum Blood, its Clotting Mechanism and Relationship to the Peripheral Blood Picture", *Amer. J. med. Sci.*, 213: 463.

BARNETT, V. H., and CUSSEN, C. A. (1954), "Acquired Afibrinogenæmia Complicating Pregnancy; Report of 2 Cases of Concealed Accidental Hæmorrhage Treated by Human Fibrinogen", *Brit. med. J.*, 2: 676.

BARRY, A. P., GEOGHEGAN, F., and SHEA, S. M. (1955), "Acquired Fibrinopenia in Pregnancy", *Brit. med. J.*, 2: 287.

BOYD, J. F. (1958), "Two Possible Cases of Acquired Hypofibrinogenemia in the Newborn", *Surg. Gynec. Obstet.*, 106: 2.

DREVERMANN, E. B., personal communication.

HODGKINSON, C. P., *et alii* (1955), "Hypofibrinogenemia and Defects of Coagulation", *Obstet. and Gynec.*, 5: 465.

HOPKINS, C. M., personal communication.

KLEIN, M., BISKIND, J. I., and SILVERBERG, A. (1956), "Post-Partum Hemorrhage Due to Depletion of Fibrinogen from Circulating Blood Stream", *Amer. J. Obstet. Gynec.*, 71: 51.

LEWIS, T. L. T. (1956), "Progress in Clinical Obstetrics and Gynæcology", Churchill, London: 293.

MCBRIDE, W. G. (1958), "The Acute Defibrination Syndrome in Obstetrics", MED. J. AUST., 1: 627.

PRITCHARD, J. A., and RATNOFF, O. D. (1955), "Studies of Fibrinogen and Other Hemostatic Factors in Women with Intrauterine Death and Delayed Delivery", *Surg. Gynec. Obstet.*, 101: 467.

SAWITSKY, A., and PLOTKIN, D. (1955), "Hypofibrinogenemia and Post-Partum Hemorrhage", *N.Y. St. J. Med.*, 55: 1153.

SCHNEIDER, C. L. (1952), "Rapid Estimation of Plasma Fibrinogen Concentration and its Use as a Guide to Therapy of Intravascular Defibrination", *Amer. J. Obstet. Gynec.*, 64: 141.

SCHNEIDER, C. L. (1954), "Obstetric Shock. Some Independent Problems of Coagulation", *Amer. J. Obstet. Gynec.*, 4: 3.

STOUFFER, J. C., *et alii* (1958), "Hypofibrinogenemia and the Placenta", *Amer. J. Obstet. Gynec.*, 75: 2.

TOWNSEND, L. (1957), "Premature Separation of the Normally Implanted Placenta. An Analysis of Management and Results", *Obstet. and Gynec.*, 105: 534.

WEINER, A. E., REID, D. E., and ROBY, C. C. (1950), "Coagulation Defects Associated with Premature Separation of the Normally Implanted Placenta", *Amer. J. Obstet. Gynec.*, 60: 379.

YAHIA, C., *et alii* (1958), "Acute Leukemia in Pregnancy", *Obstet. Gynec. Surv.*, 1: 1.

Reports of Cases.

A CASE OF CARDIAC ARREST ASSOCIATED WITH THE USE OF LIGNOCAINE ("XYLOCAINE").

By BRYAN HARTLEY,
Surgical Registrar, Launceston General Hospital.

Clinical Record.

THE patient was a man, aged 42 years, who had had the following previous operations: 1947, amputation of the terminal phalanx of the left great toe; 1949, right nephrectomy for adenocarcinoma of the upper pole, proven macroscopically and microscopically; 1955, partial gastrectomy and gastro-duodenectomy for prepyloric peptic ulcer; 1956, arthroplasty (insertion of vitallium cup) of the right hip for osteoarthritis; 1957, removal of the vitallium cup—the wound had become chronically infected and formed a discharging sinus. After this last operation he was discharged from hospital wearing a right hip spica, and was progressing well.

On the evening of the admission in question (December 1, 1957) he had become drunk and had fallen heavily. The upper edge of the plaster spica had been driven very forcibly under his left costal margin. Urine had been passed after the accident, but was not blood-stained. On examination, tenderness and rigidity were found on the left side of the abdomen. A diagnosis of ruptured spleen was made, and a laparotomy was performed. Blood was present in the peritoneal cavity. A contused left kidney (i.e., his remaining one) was found, with a fairly large rent in its substance. The laceration was sutured and the capsule brought together over the rupture. The wound was drained.

After the operation he developed a urinary fistula, but did well until the fifteenth day, when suddenly his abdominal wound burst. He was taken to the operating theatre for repair under local anæsthesia, having been pre-medicated with "Omnopon" and scopolamine. Approximately 90 ml. of 1% lignocaine solution were injected around the wound. No epinephrine had been added to the solution. The operation was almost completed when the patient suddenly had three successive epileptiform convulsions. He became cyanosed, and after about 45 seconds the anæsthetist reported that he could not feel a pulse or hear a heart beat. After a further 30 seconds the chest was opened through the fourth left intercostal space, and the heart was exposed by incision of the pericardium; it was quite still and felt flaccid. Massage was started, and a few irregular beats were soon apparent. One millilitre of 1:1000 adrenaline tartrate solution was injected directly into the left ventricle; almost immediately afterwards the heart resumed a normal forceful rhythm. The chest wound was closed with drainage, and the abdominal repair was completed.

Afterwards the patient was rather drowsy for 24 hours, but gradually recovered. He subsequently developed some infection of the chest and abdominal wounds, but both these and the urinary fistula cleared up well. He was discharged from hospital on January 23, 1958. As far as could be determined he had no ill effects due to the cardiac arrest. He has been followed up since then, and is doing well except for his hip, which is still very painful.

Discussion.

The often quoted maximum dose of lignocaine is one gramme—i.e., 100 ml. of 1% solution. However, this case illustrates that this quantity can cause very serious systemic reactions. From this experience I have learned that when lignocaine is used to infiltrate large areas, one should (i) use a 0·5% or 0·25% solution, (ii) use a mixture of lignocaine and epinephrine (1:100,000) to delay absorption, (iii) give some form of barbiturate—e.g. sodium pentobarbitone—in the premedication, as it antagonizes the central effect of the local anæsthetic.

Summary.

A case of successful cardiac massage is reported. The arrest followed infiltration with lignocaine. An additional feature of interest is that the patient survived a laceration of his only kidney; the other had been removed eight years previously when it was found to contain an adenocarcinoma.

OPERATIONS FOR PEPTIC ULCER—AN AFTERMATH.

By ATHOL ROBERTSON,

Senior Physician, South Brisbane Hospital, South Brisbane, Queensland.

A RECENT review of operations performed for peptic ulceration (Yeates and Shannon, 1958) indicates that partial gastrectomy is performed for adequate reasons and with excellent immediate results on many hundreds of patients in Australia each year. The above-mentioned review specifically excluded a discussion on complications occurring at a later date, and it is the object of this article to suggest that if partial gastrectomy is practised at the present rate, the complication of anæmia and subacute combined degeneration may be a significant problem. Standard textbooks of surgery mention the possibility, but do not emphasize that it may lead to invalidism, nor has the writer gained the impression that surgeons bear the possibility in mind when reviewing their cases subsequently.

The following clinical histories illustrate the occurrence of severe neural symptoms and anæmia occurring in patients subjected to partial gastrectomy for good reasons and with technical skill.

Case I.

A male patient, aged 48 years, a fitter and turner, was admitted to the Brisbane General Hospital on March 6, 1957, because of progressive weakness, anorexia, dyspnœa and palpitations. He had all the symptoms and signs of subacute combined degeneration of the cord. A blood examination gave the results set out in Table I.

TABLE I.

Date (1957).	Hæmoglobin Value. (Grammes per 100 Ml.)	White Cells per C. Mm.	Reticulocytes. (Percentage of Red Cells.)	Comment.
March 7	5·3	3200	—	Blood film: anisocytosis, macrocytes, occasional nucleated red cells.
March 9	—	—	0·6	Cyanocobalamin therapy commenced.
March 12	5·6	3500	0·1	—
March 19	7·4	—	12·7	—
March 25	7·5	9500	2·5	Blood film: red cells, macrocytic and hypochromic.

This patient had had an extensive subtotal gastrectomy performed at a London teaching hospital in December, 1948, for a lesser curve gastric ulcer just below the cardia, and an associated duodenal ulcer. The pre-operative blood examination gave normal results, and free hydrochloric acid was present in the stomach. On March 14, 1957, an X-ray examination with a barium meal revealed "total gastrectomy, no evidence of ulcer or stricture". He was discharged from hospital on March 26, somewhat improved, but the neuropathy was unchanged. He then attended an out-patient clinic for regular injections of cyanocobalamin, but the results of subsequent blood examinations are not known.

He was admitted to the South Brisbane Hospital on August 9, 1957, for intensive therapy, in the hope that his florid neuropathy would be sufficiently relieved to enable him to resume his trade. His hæmoglobin value on admission to hospital was 11·5 grammes per 100 ml. The white blood cells numbered 12,400 per c.mm., the differential count being normal, and a blood film revealed slight anisocytosis only. After blood transfusion and the intravenous administration of cyanocobalamin, the hæmoglobin value was 15·3 grammes per 100 ml. The patient was discharged on August 29, 1957, without any significant improvement, and arrangements were made for him to enter a rehabilitation centre. He became depressed with his inability to manipulate small articles owing to the paræsthesia of his fingers, and later was repatriated to England.

Case II.

A male patient, aged 67 years, was admitted to the South Brisbane Hospital on January 17, 1958, with pallor, fatigue, ankle œdema and paræsthesia of the hands. He had all the symptoms and signs of subacute combined degeneration of the cord. The results of blood examination are set out in Table II.

TABLE II.

Date (1958).	Hæmoglobin Value. (Grammes per 100 Ml.)	White Cells per C. Mm.	Reticulocytes. (Percentage of Red Cells.)	Comment.
January 21	7·5	—	2·1	Cyanocobalamin therapy commenced.
January 23	7·6	—	1·8	—
January 29	8·7	—	8·6	"Imferon", 100 mg. given intramuscularly.
January 30	8·6	20,000	—	Blood film: red cells normochromic, anisocytosis and macrocytes present.
February 10	10·4	12,300	—	—

When admitted to hospital, the patient was so ataxic he could not walk without support and was unable to feed and dress himself. When he was examined as an out-patient in May, he could walk at least 200 yards without support, and dress and feed himself. The findings on blood examination were within normal limits.

This patient had, in October, 1957, been subjected to a total gastrectomy, splenectomy, partial duodenectomy and pancreatectomy for an adenocarcinoma of the body of the stomach. Before operation there were no significant symptoms of neuropathy.

Case III.

A male patient, aged 54 years, was admitted to South Brisbane Hospital on March 6, 1958, with pallor, fatigue, ankle œdema and angina. He was a watch repairer and noticed some difficulty in fine manipulations with the fingers owing to the presence of paræsthesia. The results of blood examinations were as follows. On March 10, the hæmoglobin value was 5·8 grammes per 100 ml., the white cells numbered 10,200 per cubic millimetre, and in a blood film the red cells were seen to be normocytic and macrocytic. On March 14, the percentage of reticulocytes was 1·0, and cyanocobalamin therapy was begun. The reticulocyte percentages subsequently were as follows: March 17, 6·3; March 18, 20; March 19, 46; March 20, 37; March 21, 32. Histamine-fast achlorhydria was present. A barium-meal X-ray examination on March 12 was reported on as follows: "Pólya type partial gastrectomy. Good stomal function. No ulceration seen."

He was discharged from hospital on March 25, much improved, and when he was examined as an out-patient in June he looked well and felt well, and stated that he was

free of paræsthesia. The results of blood examination were normal. Partial gastrectomy had been performed eleven years previously for a gastric ulcer.

Comment.

Addison's anæmia is due to deficient secretion of intrinsic factor, which is produced in the fundus and cardia of the stomach. Thus total or partial gastrectomy, including this area, may reasonably be expected to produce megaloblastic anæmia when the body stores of cyanocobalamin have been sufficiently reduced. A subsequent or coincidental onset of peripheral neuritis and combined degeneration of the spinal cord is an accepted complication of Addison's anæmia, and when it is of such severity as in Cases I and II, the prevention is a matter of some importance. Only in Case I was there evidence of free hydrochloric acid in the stomach pre-operatively, which made the diagnosis of latent Addison's anæmia unlikely. In Cases II and III the disorder may well have been destined to develop eventually, and the gastric surgery may have merely accelerated the process. In Case II, a patient with an excellent surgical result became a medical invalid, to be restored by unspectacular therapy to an adequate physical status. In Case I, the complicating neuropathy was severe and apparently irreversible, so that the patient could not continue his trade, and chose to be repatriated rather than be trained for another less well paid occupation.

Many hundreds of gainfully occupied middle-aged men and women have had gastrectomies performed, and a review of such patients five to 10 years after operation may show that such complaints as "neuritis" and "poor circulation" are due to the insidious onset of cyanocobalamin deficiency, which will be recognized eventually when reversal is less complete with therapy. Future laboratory tests may enable the cyanocobalamin content of plasma to be readily assessed and a critical level for the commencement of replacement therapy evaluated.

It is submitted that awareness of the complication is the only method of prevention, and the words of Edward VII are appropriate: "If preventible, why not prevented?"

Summary.

Radical gastric resection is a well-established and widely performed operation, and may precipitate or aggravate a deficiency of intrinsic factor. After a period of months or years, the neuropathy of subacute combined degeneration of the cord may appear and lead to invalidism. The treatment is by the early and adequate parenteral use of cyanocobalamin.

Acknowledgements.

Permission to publish cases from the records of the Brisbane General Hospital and the South Brisbane Hospital has been given by Dr. A. D. Pye and Dr. O. Powell.

Reference.

YEATES, D., and SHANNON, R. (1958), "Review of 1094 Operations for Peptic Ulcer", MED. J. AUST., 1: 672.

BILATERAL LOSS OF VISION COMPLICATING MITRAL STENOSIS.

By R. L. HOCKIN, M.B., B.S. (Queensland), V. E. SAMPSON, M.C., M.B., B.S. (Melbourne), M.R.C.P. (London), M.R.A.C.P., AND J. M. SUTHERLAND, M.D. (Glasgow), M.R.C.P. (Edinburgh), M.R.A.C.P.,

From The Brisbane Hospital and Department of Medicine, University of Queensland.

BILATERAL loss of vision resulting from cerebral infarction is uncommon, and its occurrence is not mentioned in many standard textbooks. In a recent survey, however, Sir Charles Symonds and Dr. Ian MacKenzie (1957) reported 49 cases from the literature and added a further nine. We now report the case of a patient suffering from rheumatic heart disease, in whom loss of vision in both eyes was followed by partial recovery.

Clinical Record.

The patient, a man aged 48 years, was a grazier. He was admitted to the Brisbane Hospital on March 19, 1958. Some two hours previously he had suddenly and simultaneously lost vision in both eyes. Accompanying the loss of sight, he experienced severe pain in the right retro-orbital, right frontal and occipital regions. This was associated with giddiness and vomiting, and although consciousness was not lost, he felt dazed and confused.

He had previously suffered from rheumatic fever at 11, 16 and 17 years of age. His medical history was otherwise not relevant; in particular he had never before suffered from a similar illness and had no previous history of visual upset.

On examination the patient was well orientated and cooperative, but was worried and anxious about his condition. Headache was severe, and during the initial examination he vomited on repeated occasions. His temperature, pulse rate and respiration rate were normal. In the nervous system the pupils were equal, of average size and reacted briskly to light. Vision was absent in the left half fields and in the right was restricted to a vague perception of bright light. No reflex blinking occurred to menace. Ophthalmoscopic examination disclosed no abnormal features. The eyes moved well in all directions, and the functions of the other cranial nerves were normal. Tests of cerebellar function were performed adequately. Muscle tone and power were normal. The tendon reflexes of the left arm and leg were slightly depressed, but the abdominal skin responses were active and the plantar responses were flexor. Vibration, light touch and pin-prick sensibility were impaired in the left arm and over the left side of the trunk to the level of the anterior superior iliac spine; cortical sensation was intact. Flexion of the neck occasioned discomfort, but there was no true nuchal rigidity, and Kernig's sign was negative. In the cardiovascular system the heart rate was average, but the rhythm was irregular due to atrial fibrillation. A diastolic murmur was audible at the mitral area. The blood pressure was 160/100 mm. of mercury. Physical examination did not reveal any other abnormality.

Investigations.

Röntgenoscopy of the chest disclosed moderate enlargement of the left auricle with calcification in the mitral valve. The lung fields were clear. Electrocardiography confirmed the presence of atrial fibrillation. Lumbar puncture furnished a clear fluid under 100 mm. pressure. There was no evidence of block, and the cell count did not show any pleocytosis. The protein content was 50 mg. per 100 ml.; the Wassermann reaction was negative. The blood sugar level was 99 mg. per 100 ml.

Analysis of the urine revealed a specific gravity of 1026; there was an acid reaction, and no abnormal constituents were present on chemical and microscopic examination. No abnormal constituents were found in the stomach washings. The urinary lead content was 0·1 part per million. Bilateral carotid angiograms resulted in good filling of the anterior and middle cerebral arteries on each side. Posterior communicating and posterior cerebral arteries were not visualized. No abnormalities were seen. On the advice of Sir Charles Symonds (personal communication) vertebral angiography was not performed.

Treatment and Progress.

A diagnosis of rheumatic mitral stenosis, atrial fibrillation and occipital lobe infarction due to embolism was made. Anticoagulant therapy was commenced on March 20, some 30 hours after the onset of the acute illness.

Figures I to III (perimeter and scotometer charts) demonstrate the changes which occurred in the visual fields. On March 21, two days after the onset, the patient could dimly discern movement in the right lower quadrants of the visual fields, and by March 28 the field defect was a left homonymous hemianopia with vision in the right half fields limited to appreciation of colours and large objects.

By April 19 vision in the right half fields was 6/12 with an absolute left homonymous hemianopia. At no time was visual agnosia, visual hallucinations or denial of blindness encountered.

Vomiting ceased after the first 24 hours, but headache persisted for some 10 days. The reflex and sensory signs could not be elicited 48 hours after his admission to hospital.

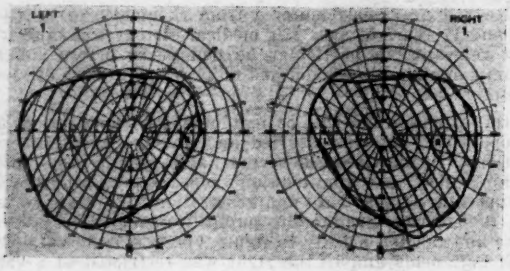

FIGURE I.

Discussion.

A cerebrovascular lesion may result in hemianopia, which remains unrecognized by the patient. A second vascular lesion affecting the other hemisphere can, in such circumstances, result in bilateral visual loss. In the present instance the patient was examined by an oculist shortly before the onset of this illness. The only defect found was a mild degree of hypermetropia. There is thus no evidence to suggest that he had a preexisting embolic cerebrovascular lesion, and that blindness resulted from further embolism to the other hemisphere.

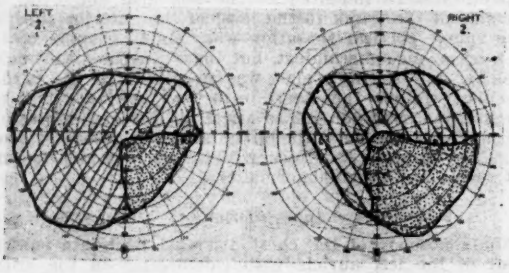

FIGURE II.

The sudden onset of visual loss suggested hysteria, an acute toxic or infective process, or a vascular lesion.

The occurrence in hysteria of sudden blindness associated with normal pupillary reactions and ophthalmoscopic appearances has been discussed by Tyrer (1957). Hysterical blindness may also occur as a perpetuation of the transitory visual impairment associated with syncope or head injury (Brain, 1955). In such instances the differential diagnosis between hysteria and organic disease may present considerable difficulty. In the hysteric, obstacles placed in the patient's path may be avoided and reflex blinking may occur to menace. Sometimes, however, such tests are inconclusive, and the diagnosis becomes apparent only after several days of careful surveillance. The mental attitude of the present patient to his symptoms, the associated headache and vomiting and the absence of reflex blinking to menace did not favour a diagnosis of hysteria. The course of events subsequent to the ictus confirms this opinion.

Complete blindness may occur after a relatively small dose of quinine is taken (Smith, 1934). The pupils in such cases are usually dilated and immobile and the fundi commonly present a pale ischæmic appearance. Similarly, lead and arsenic may cause amblyopia, and methyl alcohol characteristically occasions blindness at an interval varying from a few hours to several days after ingestion (Locket, 1957). In the present case there was no evidence suggestive of exposure to such toxic substances.

In neuromyelitis optica, optic neuritis not infrequently precedes any evidence of myelitis, and in some instances visual impairment may be the sole manifestation of the disease (Scott, 1952). In cases which show marked reduction of visual acuity, widely dilated immobile pupils are the rule (Duke-Elder, 1940), but according to Scott, quite marked impairment of vision can occur with amazingly little loss of the light reflex. The characteristic field defect is bilateral central scotoma, but homonymous defects have been described (Brain, 1955). In Scott's experience there is generally some degree of papillitis,

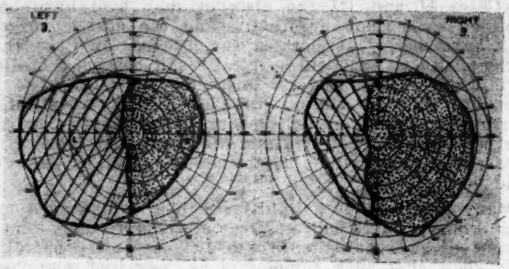

FIGURE III.

and McAlpine (1938, 1955) states that in over 50% of cases the cell count or protein content of the cerebro-spinal fluid is abnormal.

The evidence did not therefore favour a diagnosis of neuromyelitis optica, whereas the dramatic onset and the demonstrable source of an embolus strongly suggested a vascular ætiology. The clinical picture was considered compatible with an embolus lodging at the bifurcation of the basilar artery and shedding secondary fragments in a symmetrical fashion to the calcarine branches of both posterior cerebral arteries.

The posterior cerebral arteries supply the mid-brain, the superior cerebellar peduncles, the posterior half of the thalamus, the retrolenticular portions of the internal capsules, the inferior surface of the temporal lobes and the medial and inferior aspects of the occipital lobes. It might therefore be expected that occlusion of one or both posterior cerebral arteries would produce a widespread neurological deficit. However, as pointed out by Elliot (1953), the complete clinical picture is rare, since the mid-brain and superior cerebellar peduncles have an adequate collateral circulation derived from the basilar and posterior communicating arteries. Similarly, Symonds and MacKenzie (1957) emphasize that occlusion of the posterior cerebral arteries can be compensated for by anastomotic channels from the middle cerebral as well as from the posterior communicating arteries; but no similar mechanism exists with regard to the smaller cortical arterioles, since within the brain substance cerebral arteries are end arteries (Brain, 1957). Brain also emphasizes that there is a functioning antero-posterior anastomosis in each posterior communicating artery. Thus, if the carotid system was maintaining an adequate collateral circulation, one would have expected the posterior communicating arteries to have been visible on carotid angiography. Since this was not the case it seems likely that the block at the basilar bifurcation was incomplete, or that, at the time of angiography, the obstruction was entirely distal to the junction of the posterior cerebral and posterior communicating arteries. This would not prevent symptoms referable to the blocking of small end arteries in the calcarine cortex by minute fragments derived from the primary embolus.

The symptomatology presented by this patient is in accord with that described by Symonds and MacKenzie. The sudden onset is not usually accompanied by loss of consciousness and mental confusion; headache and vomiting are not infrequent. Complete blindness, although persisting in about one quarter of cases, is generally succeeded by various visual field defects including, in some cases, hemianopia. Psychical visual symptoms—an inconstant feature—were not encountered in this case.

Summary.

A case of occipital lobe infarction presenting with loss of vision in both half fields is reported in a patient suffering from mitral stenosis and atrial fibrillation.

The visual loss was regarded as being due to an embolus lodging at the bifurcation of the basilar artery with secondary occlusion of the calcarine branches of the posterior cerebral arteries.

Anticoagulant therapy coincided with considerable improvement, the final field defect being an homonymous hemianopia.

Acknowledgement.

It is a pleasure to thank Sir Charles Symonds for his interest and advice.

References.

BRAIN, W. R. (1955), "Diseases of the Nervous System", 5th edition, Oxford University Press, London.

BRAIN, W. R. (1957), "Order and Disorder in the Cerebral Circulation", *Lancet*, 2: 857.

DUKE-ELDER, W. S. (1940), "Textbook of Ophthalmology", Volume 3, Kimpton, London.

ELLIOT, F. A., HUGHES, BRODIE, and TURNER, J. W. A. (1953), "Clinical Neurology", Cassell, London.

LOCKET, S. (1957), "Clinical Toxicology", Kimpton, London.

MCALPINE, D. (1938), "Familial Neuromyelitis Optica: Its Occurrence in Identical Twins", *Brain*, 61: 430.

MCALPINE, D., COMPSTON, N. D., and LUMSDEN, C. E. (1955), "Multiple Sclerosis", E. and S. Livingstone, Edinburgh and London.

SCOTT, G. I. (1952), "Neuromyelitis Optica", *Amer. J. Ophthal.*, 35: 755.

SMITH E. C. T. (1934), "Quinine Amblyopia", MED. J. AUST., 2: 289.

SYMONDS, C., and MACKENZIE, I. (1957), "Bilateral Loss of Vision from Cerebral Infarction", *Brain*, 80: 415.

TYRER, J. H. (1957), "The Differentiation of Hysteria from Organic Neurological Disease", MED. J. AUST., 1: 566.

Notes on Books.

The Indian Year Book of Medical Sciences, 1958. Edited by Madhusudan M. Desai, M.D., F.C.P.S., F.R.F.P.S.(G.), D.T.M.H. (Eng.), Dhirubhia B. Doshi, M.R.C.P., D.T.M.H. (Eng.), and Noshir H. Wadia, M.D., M.R.C.P. (Lond.); 1958. Bombay: Current Technical Literature Company, Private, Limited. 9½" x 7", pp. 530, with many illustrations. Price: 75s.

IN the preface it is stated that this book has two main objects, the first to provide the Indian medical practitioner, within the compass of a single volume, with information on recent advances in medical sciences, in view of the fact that hundreds of doctors practising in rural areas have little contact with academic medicine and no opportunities to attend refresher courses. The second object is to give due emphasis to investigations and observations made in India. The present volume, which is the first of its series, is intended as a review of scientific work done in the various branches of medicine, both in and out of India, during the last few years. It is intended that subsequent volumes should each cover the advances of the year preceding its publication.

The result is a volume containing about 200 contributions, ranging from short abstracts of individual papers to comprehensive discussions of some length, with a full list of references at the end. The contributors are apparently all Indian doctors, but the papers referred to are widely selected, with proper emphasis on matters of special interest to Indian practitioners. All contributions are in the English language, and they are arranged in alphabetical order, according to their titles. This volume appears to fulfil its primary purpose very adequately, and its editors are to be congratulated on having rendered a valuable service to their practitioner colleagues.

Acta Leidensia: Edita Cura et Sumptibus: Scholæ Medicinæ Tropicæ. Volume 28, 1958. Universitaire Pers Leiden. 9½" x 6", pp. 170, with many tables and figures. Price not stated.

THIS latest collection of articles from the school of tropical medicine of the University of Leyden is further proof of the quality of the work emanating from that centre. The great majority of the contributions are in the English language. The first and longest is a fifty-page monograph by A. B. Stam on *Entamœba invadens*, a species which is morphologically almost indistinguishable from *E. histologica*, but which is a parasite of reptiles and is adapted to an optimum temperature of 23° to 25° C. Its study shows some interesting parallels with *E. histolytica*. The life history of the two species is identical; both may be the cause of acute disease in their respective hosts, or they may exist as harmless inquilines, causing no discernible symptoms, and the author discusses the behaviour of *E. histolytica* in the light of his observations on *E. invadens*. He suggests that old-world monkeys were the original hosts of *E. histolytica*, and that the normal hosts of *E. invadens* are members of the crocodile family. (*E. invadens* came to light as a disease of reptiles in zoos, both in Europe and in America.)

The remaining communications are less recondite, dealing with a wide variety of topics, and are reprints of articles and other communications, issuing from the Leyden school of tropical medicine, which have already been published elsewhere, mainly in sources not readily accessible to English and American workers.

Ciba Foundation Symposium on the Neurological Basis of Behaviour, in Commemoration of Sir Charles Sherrington, O.M., G.B.E., F.R.S., 1857-1952. Editors for the Ciba Foundation, G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Cecilia M. O'Connor, B.Sc.; 1958. London: J. and A. Churchill, Limited. 8" x 5", pp. 412, with 109 illustrations. Price: 52s. 6d. (English).

THIS volume is a collection of the papers read at a symposium on the neurological basis of behaviour, which was organized by the Ciba Foundation in July, 1957, to commemorate the centenary of the birth of Sherrington. The symposium was held in London, and was arranged to fit in with international congresses in neurological sciences which were held in Brussels about the same time. As is usual at the Ciba Foundation, in the interests of thorough discussion of the subject the group participating was relatively small, but it included authorities in neurophysiology and related fields from British, American and Continental centres. Australia was represented by Professor J. C. Eccles, who read a paper on "The Behaviour of Nerve Cells". In all, 19 papers are included, and each is accompanied by a report of the discussion which followed. The first paper is an historical survey of the early development of ideas relating the mind with the brain, illustrated by reproductions of fifteenth and sixteenth century figures, by H. W. Magoun of Los Angeles. The remaining papers deal with current research into many aspects of neurophysiology, and are by leading authorities in their subjects. The volume is well illustrated with plates and diagrams.

Queensland's Health. Journal of the Department of Health and Home Affairs, 1959. Volume 1, Number 1 (April); Government Printer, Brisbane.

AN appropriate contribution to the celebration of Queensland's centenary is the launching of a journal by the Department of Health and Home Affairs of that State, under the title of *Queensland's Health*. In his foreword, Dr. H. W. Noble, Minister for Health and Home Affairs, summarizes the work of his department as follows:

> My Department controls public hospitals and mental hospitals throughout the State. In addition, it exercises control on communicable diseases, on foods and drugs, on the sanitation of the environment, on tuberculosis, on industrial medicine, on maternal and child care, ad on the health of school children. In addition, the Laboratory of Micro-Biology and Pathology provides a first-class service in clinical pathology and in public health bacteriology, whilst the Government Chemical Laboratory undertakes analyses of all kinds of foods, articles, and substances.
>
> I feel it is appropriate that some of the work performed by the various sections of my Department

should come to your notice through these pages from time to time. The new knowledge thus gained must benefit the health of the people of this State.

This little journal is designed primarily to interest lay readers; but if succeeding issues are as interesting as the first, medical practitioners will read it with pleasure. In this number there are 10 articles, all by experts in their own fields. It is encouraging to see that history has not been neglected, and from this point of view we commend the articles entitled "History and Health in Queensland—The Convict Era", by Dr. P. R. Patrick, "Looking Backwards in Preventive Medicine", by Professor Douglas Gordon, and "School Dentistry in Queensland", by T. D. Pugh. For the rest, the format is pleasing and the type is clear and readable.

Mental Disorders. By W. S. Dawson; Fifth Edition; 1958. Edinburgh and London: E. and S. Livingstone, Limited. 7¾" × 5", pp. 68. Price: 2s. 6d. (English).

Most of us are familiar with the booklets of the "Catechism Series" from our student days, and the present publication gives the reader a quick run through the field of mental disorders in the form of dogmatic answers to a selection of basic questions. Whatever one may think of potted medicine, to the hard-pressed student the value of such aids as a means of quick revision is undoubted. The nine pages on the legal aspects of mental disorders refer to English and Scottish Law, and will soon need revision to conform with the *Mental Health Bill* at present before the British Parliament.

The Phantom Limb. By Hamilton Johnston; 1958. London: Victor Gollanez, Limited. 7" × 4½", pp. 256. Price: 18s. 9d.

In his first novel, "The Doctor's Signature", Dr. Hamilton Johnston compounded a formula from ingredients of well-established popular appeal—of which the doctor's private life was not the least important—with considerable success, for according to the publisher's blurb, it was "one of the two best-selling first novels of 1957". In his second novel, Dr. Johnston has stuck to his original formula to the extent that the plot again concerns the private life of a general practitioner in the Welfare State, but this time he has paid considerably more attention to his characters as people, and in the first half of the book they become suspiciously like real persons. However, as the story progresses, the characters become engulfed in a thickening plot as complications succeed each other in a mounting *crescendo*, and the tidying up at the end is quite ruthlessly thorough. Dr. Johnston does not spare the sordid detail, but neither does he labour it unduly; his characters are fundamentally weak and amoral, but they are extremely plausible, and the interest of their story never falters. Dr. Johnston has again succeeded in turning out a story which can be confidently recommended as entertaining light reading, and it seems safe to predict that in it he will repeat his first success.

Science News. No. 49, edited by Archie and Nan Clow. 1958. Victoria: Penguin Books Pty. Ltd.; The Whitefriars Press, Limited. 7" × 4", pp. 128, with illustrations. Price: 4s.

Science News. No. 50, edited by Archie and Nan Clow; 1958. Mitcham, Victoria: Penguin Books Pty. Ltd. 7" × 4", with illustrations. Price: 4s.

In attaining its first half century, "Science News" is to be congratulated on the useful contribution it has made in recent years in providing the informed layman with authoritative reports on advances in many varied fields of scientific research. From the nature of their subject matter, these reports cannot be classed as simple or elementary scientific reading, but the continued popularity of these volumes is encouraging evidence of the existence of a public with sufficient basic scientific knowledge and interest in scientific developments to create a demand for relatively advanced information of the type here provided.

The present two volumes each contain six articles on a wide variety of topics, a "research report" consisting of short notes on recent developments in various fields, and book reviews. Articles in number 49 include "Unconventional Production of Foodstuffs", "Silicones", "The Stuff of Bones", and "Communication in the Field of Science". Number 50 begins with a very interesting account of the voyages of H.M.S. *Beagle*, setting out the little-known background of Darwin's famous voyage. Other articles include "A Sceptical Chemist" in which the author puts the old idea of vitalism in a modern setting, and a biochemical essay on the metabolism of drugs. The research report includes an interesting annotation on meteorite craters.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Reminiscences and Adventures in Circulation Research", by Carl J. Wiggers, M.D.; 1958. New York and London: Grune & Stratton, Incorporated. 9" × 5¾", pp. 416, with 82 illustrations. Price: $9.75.

Memoirs of an investigator.

"Curare and Curare-Like Agents", edited by D. Bovet, F. Bovet-Nitti and G. B. Marini-Bettòlo; 1959. London: D. Van Nostrand Company, Limited; Amsterdam, London, New York and Princeton: Elsevier Publishing Company. 9¼" × 6¼", pp. 478, with many illustrations and tables. Price: 85s. (English).

This volume constitutes the proceedings of the International Symposium on Curare and Curare-Like Agents held in Rio de Janeiro in August, 1957. Some papers are in English, some in French.

"The Child's World", by Phyllis Hostler. 1959. Mitcham, Victoria: Penguin Books. 7" × 4", pp. 205. Price: 4s.

The aim of this Penguin Handbook is "to show why children behave as they do and how we can make our behaviour intelligible to them".

"The Nature of Stress Disorder". London: Hutchinson Medical Publications. 8½" × 5½", pp. 300, with 20 illustrations and 32 tables. Price: 25s. (English).

Papers read at the conference of The Society for Psychosomatic Research held at the Royal College of Physicians, May, 1958.

"Individual and Familial Dynamics", edited by J. H. Masserman, M.D.; First Edition, 1959. New York, London: Grune and Stratton. 8½" × 5½", pp. 224. Price $6.75.

Volume II in the "Science and Psychoanalysis" series.

"The Hand: Its Anatomy and Diseases", by John J. Byrne, M.D.; 1959. Oxford: Blackwell Scientific Publications. 9" × 6", pp. 398, with 165 illustrations. Price: 80s. (English).

This book deals with all aspects of the subject: structure and development, infection, trauma, other diseases and reconstructive surgery.

"Vascular Spiders and Related Lesions of the Skin", by William Bennett Bean, M.D.; 1959. Oxford: Blackwell Scientific Publications. 9" × 6", pp. 392, with 130 illustrations. Price: 63s. (English).

A book based on extensive personal observation and experience.

"Medical Museum Technology", by J. J. Edwards and M. J. Edwards, 1959. London: Oxford University Press. 8¾" × 5½", pp. 186, with many illustrations. Price: 39s. 3d. (English).

The author, who is Chief Technologist at the London Hospital Medical College Museum, deals with the history of the subject as well as with modern techniques.

"Dangerous Marine Animals", by Bruce W. Halstead, M.D.; 1959. Cambridge and Maryland: Cornell Maritime Press. 9" × 5¾", pp. 160, with 86 illustrations. Price: 30s. (English).

The author aims "to provide persons, encountering dangerous marine animals, with a ready source of identification, geographical distribution, habits and noxious characteristics of these animals".

"The Kansas Doctor: A Century of Pioneering", by Thomas Neville Bonner; 1959. Lawrence: University of Kansas Press. 9" × 6", pp. 352, with illustrations. Price: $5.00.

The story of medicine in Kansas.

The Medical Journal of Australia

SATURDAY, AUGUST 8, 1959.

RAYMOND DART AND THE ORIGIN OF MAN.

THE recent retirement of Professor Raymond Dart from the Chair of Anatomy at the University of Witwatersrand at the end of a term of 35 years provides a suitable occasion on which to reflect on the great developments which have taken place in our knowledge of the origins of man in that time, developments to which Professor Dart himself contributed so largely with objectivity and distinction. Professor Dart is the distinguished pupil of a great master, Sir Grafton Elliot Smith. Like Elliot Smith, Dart was a graduate of the University of Sydney, and had worked in the Department of Anatomy under Professor James T. Wilson. Later, after the end of the first World War, Dart spent a year working under Elliot Smith, then Professor of Anatomy at University College, London. After a year in America as one of the first holders of a Rockefeller Foundation Fellowship, he accepted the Chair of Anatomy at the University of Witwatersrand, taking up his appointment in January, 1923.

The foregoing biographical details are taken from a sketch by T. V. Tobias in a special commemorative issue, dated November, 1958, of *The Leech*, the domestic medical journal of the University of Witwatersrand, in which is published a collection of articles by distinguished anthropologists from many countries, contributed in honour of Professor Dart's retirement. According to Tobias, Dart's first love was neurology, but circumstances forced him into the role of one of the leading authorities on fossil man, for within a few months of his arrival in South Africa there came into his hands a specimen which has become a milestone in the history of fossil man. This specimen, the Taungs skull (subsequently designated *Australopithecus*) was a substantial part of the skull of a near-human child. At that time ideas on fossil man were still largely based on what had been found in Europe, and the attention of those who looked for the focus of the origin of man was directed to Eastern Asia, where, in 1891, Dubois had found the remains of the ape-man of Java (*Pithecanthropus erectus*). It had seemed that, as far as man was concerned, Africa had little to contribute to the fossil record, and though Dart himself had no doubt that the Taungs fossil represented a true Hominid, his claims were at first received with some scepticism. However, the Taungs discovery was soon followed by other finds, and it has since become clear that a few hundred thousand years ago several different species of ape-men roamed the South African plains. It may never be possible to say where true man first appeared, but the great importance of the South African finds to the study of the evolution of man cannot be denied.

To the early evolutionists who claimed that man was descended from an ape, the picture, with the limited data available to them, may have seemed relatively simple. Since then, the large number of finds of the remains of early man and his precursors has shown how enormously complex the situation really is. It is no longer possible to say of any one fossil that this is the missing link. The human family (Hominid) tree can be traced back a surprisingly long way in geological time, as a line quite distinct from that of the great apes (Pongids); but this line is not a simple one: rather is it a tree of innumerable branches, of which we have been able to gather but the impressions of a twig here and there. It is a fascinating exercise to attempt to reconstruct the tree from the admittedly fragmentary evidence. Though there is a considerable element of speculation in such attempts, the fossil evidence is such that there is no scientific doubt that modern man was preceded by a great variety of primitive Hominids, inferior to man in the development of the brain and showing various other "primitive" features, but with man-like features which distinguish them clearly from the Pongids.

The past fifteen years have seen a remarkable development of techniques for determining the ages of fossil specimens. Previously, estimations of age were based on indirect evidence such as stratigraphical position and the thickness of sediments, but with new methods depending on estimations such as those of radioactive carbon, fluorine replacement or the potassium/argon ratio, fossil remains can now be dated with a considerable degree of accuracy. This has provided a tool for testing the conclusions of early anthropologists, and a means of obtaining a much clearer picture of the sequence of recent geological events. The earliest fossil for which a place in the Hominid tree has been seriously considered is Oreopithecus, found in brown-coal beds in Tuscany. The Hominid affinities of this fossil have not been generally accepted, but the age of the beds is believed to be of the order of ten to fifteen million years. The recent report of the finding of many additional remains of this fossil promises fresh light on this controversy. However, according to K. P. Oakley[1] in an article on the dating of the stages of Hominid evolution, "the oldest known remains of unquestionable Hominidæ date from the end of Lower Pleistocene times: *Australopithecus* [the Taungs skull and other finds] in South Africa and *Pithecanthropus* from Java". Comparison with other deposits whose chronological age has been established suggests an age for these fossils approaching 500,000 years. *Pithecanthropus* was at a more advanced stage than *Australopithecus*, but, whether or not these forms were contemporary, it is probable that at a time when *Australopithecus* roamed the South African veldt, more advanced forms were already in existence. Indeed, in another article, J. T. Robinson[2] of the Transvaal

[1] *The Leech*, 1958, 28:112 (November).
[2] *Ibidem*: 94.

Museum, discusses the question of whether *Australopithecus* was a tool maker and concludes that he was probably not, but that before *Australopithecus* disappeared from the scene early took-making men had already appeared. Robinson implies that the ability to fashion stone implements should be regarded as a hall-mark of true man, and proposes that Hominids should be subdivided into the hominines, true men who knew the art of making tools, and the australopithecines or prehomines, who may have used bone and other materials as tools, but did not know how to fashion them to their needs. (Tool using, as opposed to tool making, has been recorded in some species of birds and in other animals.)

Australopithecus is exceptional among early Hominids in that a relatively large amount of fossil material is available for his reconstruction. Our knowledge of the physical nature of the earliest tool makers is limited by the fact that, though their stone tools have survived in large numbers, the human fossils which can be associated with these tools are few and very fragmentary. After *Australopithecus*, the next fossil Hominid of which any considerable quantity of material is known is Peking man, now regarded as a near relative to *Pithecanthropus* of Java. The only Hominid fossil from Europe which may represent this stage is the famous Mauer jaw, which Oakley dates with some confidence as being about 370,000 years old.

We now come to the difficult question of when *Homo sapiens* first appeared on the stage. Claims of high antiquity have been made for many finds of human bones, but few have stood up to the searching tests of modern analytical methods. Oakley mentions only two which he accepts as belonging to the Middle Pleistocene period, one from Britain (the Swanscombe skull) and one from Germany. Both fossils are very incomplete, but sufficient is preserved to indicate that they had "brains morphologically close to the modern type". Oakley, who thus refers to them, infers an age of over 200,000 years for these fossils. Carbon-14 dating, which, with modern refinements, can be used to estimate ages up to 70,000 years, makes it possible to date the remains of later palæolithic men with considerable accuracy. There is no space here to discuss the still controversial question of the status of the Neanderthal race, who lived in Europe during the last ice age, but Oakley gives data indicating that they survived up to about 40,000 years ago. In conclusion Oakley sums up the available data as indicating that:

> . . . the Hominidæ had attained the level of *Pithecanthropus* by 400,000 years ago, and the status of primitive *Homo sapiens* by 250,000 years ago, but that there is no undisputed evidence of the existence of *Homo sapiens sapiens* before about 40,000 years ago.

When we turn to our own country we realize that both the geological and the historical record of man in Australia is relatively very brief. Professor A. A. Abbie[1] has contributed an article on the original Australians, in which he surveys briefly some of the facts about the aboriginal in an effort to present him as he really is. Much of Abbie's article is taken up with a discussion of the physical characters of the aborigines, but near the end of it he gives an interesting brief discussion of the origins and antiquity of the aborigines. He points out that there is little doubt that they came from Asia, but that attempts to identify them with one or other of various primitive Asiatic races are highly speculative. He makes an interesting point when he casts doubt on the widely accepted conclusion that the admittedly distinct Tasmanians lived in Australia before the coming of the aborigines, suggesting that it is more probable that they are descendants of accidental migrants from Melanesia, and quotes N. W. G. MacIntosh as having demonstrated that wind and tide would favour such a chance landing. However, this is a point which may always remain an open question. As for the Australian aborigines, Abbie rejects the "tri-hybrid" theory of their origin, and evidently favours the opposing theory, that they can best be regarded as a product of the diversification of a single homogeneous stock. He states that the earliest radiocarbon dating yet established to indicate the antiquity of man in Australia goes back a mere 8000 years or so, and points out that this accords with the stage of their cultural evolution. E. D. Gill, in a paper read at the meeting of A.N.Z.A.A.S. in Adelaide in August, 1958, stated that radiocarbon datings in the Maribyrnong Valley, Victoria, provided evidence that man lived in Australia about 10,000 years ago, and that there was circumstantial evidence indicating the possibility that he was here about 14,000 years ago. However, this still places the first arrival of man in Australia near the close of the old stone age. There is little doubt that there is much more to be discovered about the earliest Australian immigrants, since systematic excavation of archæological sites is still in its infancy as far as Australia is concerned.

In conclusion it should be said that Professor Dart's activities have ranged far outside the study of fossil man. The tributes which have been paid to him on his retirement bear eloquent testimony to the regard in which he is held as a teacher and because of the work which he has done for the development of medical education in South Africa. We hope that he will enjoy many years of fruitful activity after the date of his official retirement.

[1] *The Leech*, 1958, 28:120 (November).

Current Comment.

CEREBRAL PALSY.

Any medical writing by R. S. Illingworth is worthy of serious study, and a new book which he has edited, and to which he has contributed, is notable.[1] In the preface it is stated that "there can be few subjects in the whole of medicine which compare with cerebral palsy for the diversity of problems which it poses in so many disciplines". To try to set out the present-day position in regard to these problems, and the most recent knowledge in regard to investigations and treatment, has been the task of the distinguished men and women who have contributed the various sections on causation, the clinical aspects, education, physical therapy, psychology, speech therapy, orthopædic surgery and neurosurgery. Illingworth himself

[1] "Recent Advances in Cerebral Palsy", edited by R. S. Illingworth, M.D., F.R.C.P., D.P.H., D.C.H.; with a foreword by Norman B. Capon, M.D., F.R.C.P., F.R.C.O.G.; 1958. London: J. and A. Churchill, Limited. 9½" × 6", pp. 404, with 136 illustrations. Price: 50s. (English).

writes on the classification, incidence and causation of cerebral palsy; on the early and differential diagnosis; and on the handicaps of the child with cerebral palsy. He points out that in Britain there are between one and two cases of cerebral palsy in every 1000 children of school age. Illingworth agrees with other writers that anoxia is probably the most important single causative factor, but makes the plea that since the known factors in the causation of cerebral palsy are for the most part identical with those underlying premature delivery, still births, neonatal deaths and mental deficiency, research into the causes of cerebral palsy should be directed to determining the cause of these wider problems. Cyril B. Courville, in discussing the structural changes in the brain in cerebral palsy, notes that Little (1843-1853) pointed out the association of asphyxia at birth with certain crippling deformities of the extremities, and that Virchow (1867) called attention to cystic degeneration of the cerebral centrum in early life, which he considered to be a form of "encephalitis". Interest in this last observation has recently been revived.

The section on early diagnosis and differential diagnosis stresses once again Illingworth's clinical acumen. Little has been written about early diagnosis of cerebral palsy, and yet every student and practitioner should be aware of its importance. It is also necessary to remember that a proportion of these children have associated hearing and seeing defects.

The psychological and educational problems of children with cerebral palsy are dealt with adequately, and the comments by Norah Gibbs on the problems of the parents are simple and sensible. The group of children, perhaps 25% of all those with cerebral palsy, who are so mentally handicapped that they cannot benefit from education at school, and who also have a moderate or severe degree of physical disability, have always presented a difficult problem. The establishment in Lanarkshire, Scotland, of a residential home for the treatment and training of these severely handicapped children represents a brave attempt to give them help. Physical and speech therapists will find much to interest and assist them in the sections devoted to these subjects, including some particularly good illustrations of equipment.

M. A. Perlstein, in the section on drug treatment, is realistic in stating that drug therapy plays a relatively small role in the treatment of cerebral palsy. Nevertheless, his discussion of the various drugs used is valuable.

G. A. Pollock and W. J. W. Sherrard contribute a very practical chapter on the question of treatment by orthopædic surgery. The actual number of conditions which can be helped here is small; nevertheless, there is no doubt that in this group of well-chosen patients satisfactory results are obtained. There is obvious need for close liaison between the physician and the orthopædic surgeon, a liaison which has not been strikingly apparent in some Australian centres.

The section on recent advances in the neurosurgery of cerebral palsy is particularly stimulating. It has been contributed by Russell Meyers, of the State University of Iowa, who is very successful in winnowing the grain from the chaff. He chides the "structure bound" physician and surgeon, commenting that their theory "perpetuates a modern version of demonology that has for so long pervaded the medical field". He argues convincingly for the "dynamic" concept of the "related neuromuscular glandular apparatus involved in the exercise of a given function" —for example, vision—and he stresses the importance of "feed backs" in this and of the information available from the electronic engineer. Viewed in this clear, scientific atmosphere, many of the operations which have been performed for cerebral palsy are manifestly useless. Even in relation to pallidotomy and pallidectomy, Russell Meyers considers that we possess little useful information on rigidity as met with in cerebral palsy. However, he discusses the encouraging results obtained by mid-brain pedunculotomy (crusotomy) and "hemispherectomy". He thinks that the recent development of an ultrasonic tool for producing lesions of any predetermined size and shape at any desired cerebral site, without damaging other sites, may open up new avenues of approach to neuroanatomical, neuropathological and neurotherapeutic problems.

One might say that the basic message of this book is the need for early and accurate diagnosis and for appropriate treatment. In Australia, as in many countries, there is keen and growing interest, due in no small measure—let it at once be said—to the persistence and organized efforts of the parents of these children. New horizons have been opened, particularly for those children who have previously been largely discarded as being ineducable. This book, with its solid factual approach, will be read with interest by those many workers in medicine and the various disciplines who have the care of these children and adults. If there is any lack in this book, it is perhaps that of a final section or epilogue which would bring together and epitomize the various facets so ably dealt with in the context, and present to the reader the composite picture of the child, the parents and their problems.

PROPERDIN.

PROPERDIN is a name which has lately begun to appear in the literature of experimental medicine, and, in our search to find out more about this obscure substance, we came upon an article by Peter A. Herbut,[1] of the Jefferson Medical College of Philadelphia, which seemed to throw some light on the subject. For some years Herbut and his colleagues have been screening chemical substances for tumour-inhibitory properties against a variety of animal tumours, and after many disappointments they concluded that it was necessary for the progress of their research to grow human tumours in experimental animals. Out of 206 human cancers tried, only one was successfully grown, in irradiated weanling rats. This caused Herbut to reflect on the natural resistance of animals to heterologous transplanted tissue, and he concluded that vague statements about "immune reaction" or "natural and acquired immunity" were quite unhelpful. Two unrelated discoveries about this time appeared to him to have some bearing on the problem. The first was the discovery by L. Pillemer, in 1954, of a new serum protein, a euglobulin, which he called properdin (Latin *perdere*, to destroy) because, in the presence of complement and magnesium ions, it was found to kill bacteria, inactivate viruses, lyse certain types of erythrocytes and kill some protozoa. It was depleted in rats subjected to total body irradiation. The second discovery was that of J. G. Kidd, who demonstrated that normal guinea-pig serum contains a substance which causes regression of certain tumours in mice. Suspecting that properdin and the tumour-inhibiting substance in guinea-pig serum might be one and the same and that properdin might be the natural tumour inhibitor of the body, Herbut carried out a series of carefully planned experiments to test this hypothesis. The results of his experiments did not support the hypothesis which inspired the investigation, but they led to some very interesting conclusions. These are: (i) Animals can be conditioned to heterologously transplanted tumours by irradiation, cortisone or zymosan (an insoluble carbohydrate). (ii) Irradiation and zymosan, in doses necessary to do this, depress the properdin level in Wistar rats but slightly. (iii) Restoration of the properdin level with human properdin in irradiated rats does not restore their resistance to heterologous transplants. (iv) The operating mechanism is thus not through the properdin system, or else the conditions of the experiment were not correct. (v) The tumour-inhibiting principle in guinea-pig serum has so far been demonstrated only in guinea-pig serum and not in other mammalian sera; some of its physical properties have been established; it has not yet been identified, but has been shown not to be complement, properdin or lipopolysaccharide. (vi) Properdin levels of sera from mice with transplanted tumours vary inversely with the growth of the tumours, but this fluctuation probably indicates the extent of tumour development rather than determines it.

[1] *Trans. Stud. Coll. Physns Philad.*, 1959, 26: 129 (February).

Abstracts from Medical Literature.

HYGIENE.

The Validity of Information Obtained in Health Surveys.

P. E. ENTEBLINE AND K. G. CAPT (*Amer. J. publ. Hlth*, February, 1959) compared the results obtained from three different methods of health-survey interviewing. In one method one member of the household supplied the required information for all other members; in the second method each member was interviewed personally; in the third method a *questionnaire* was left for each absent member to fill in and return. The results are given in detail. Rarely did the results obtained by the three methods differ significantly when investigated statistically. The authors conclude that it is difficult to generalize about biases in health information provided by household respondents regarding others in the household. These will probably vary somewhat with the characteristics of the respondent and with the nature and seriousness of the health condition or disease under consideration. The use of household respondents will probably result in the reporting of no less a total of disease, in the same broad categories, than would be the case if each adult were to be interviewed for himself.

Mottling of Teeth Enamel in the Arabian Peninsula.

M. EL. TANNIR (*Amer. J. publ. Hlth*, January, 1959) has investigated mottled teeth enamel among people living in Mecca and the Arabian Peninsula. A total of 570 persons were examined, including 68 females. Mottling was found in 70% of people examined. It consisted of deep brown, yellow, and chalky white patches. Among those who had been born and had spent their childhood in Mecca, 90% of adults and 48% of children had mottled teeth. Caries was not present in 62% of all those examined and not present in 65% of those examined who had been born and had spent their childhood in Mecca. It was not present in 55% of those who had been born and had spent their childhood outside of Mecca. The main water supply in Mecca contains 2 p.p.m. of fluorine. No evidence of periodontal disease was found in 62% of those examined, but among those who had been born and had spent their childhood outside Mecca only 45% were free of periodontal disease. The author suggests that manganese was the cause of the brown coloration of the mottled enamel, and he associates the mottling and resistance to caries and periodontal disease with the 2 p.p.m. of fluorine in the water supply.

Organic Phosphate Insecticides.

C. S. PETTY *et alii* (*Amer. J. publ. Hlth*, January, 1959) report the results of a survey of blood cholinesterase activity of Louisiana agricultural workers exposed to organic phosphorus insecticides. They analysed blood specimens from 245 farmers, crop-dusting pilots, crop insect checkers, insecticide mixers, tractor drivers and other agricultural workers for blood cholinesterase activity during the 1957 cotton crop treatment season. The total number of analyses performed was 640, of which 452 were carried out by the whole-blood screening technique of Fleisher, Woodson and Simet, and 188 by the colorimetric method of Fleisher and Pope. The actual number of persons exposed and the total amounts of organic phosphate insecticides used during the season under review are not known. Large amounts of methyl parathion and malathion, and smaller amounts of parathion, "Guthion" and demeton were used in both powder and liquid mixtures. No instance of subclinical organic phosphate insecticide poisoning was discovered in this survey, although all persons contributing blood samples were exposed in varying degree to these toxic agents. During this same season, only four cases of proved overt organic phosphate poisoning were encountered among agricultural workers in Louisiana.

Strontium-90, Iodine-131 and Other Radionuclides in Milk.

J. E. CAMPBELL *et alii* (*Amer. J. publ. Hlth*, February, 1959) have analysed milk from a number of areas in the United States of America for a number of radionuclides in an attempt to determine if there is an increase in the radioactivity of food resulting from radioactive materials created as a result of recent nuclear detonations. The methods of analyses and results obtained are given. The concentrations of iodine-131, barium-140 and strontium-89 varied widely, the higher levels being closely associated with the number of nuclear weapon tests per month in the United States, while tests conducted elsewhere in the world had a noticeable but lesser effect on the values observed. On the other hand, the values of cæsium-137 and strontium-90 were found not to be correlated with the number of concurrent weapon tests. Samples from each geographical area investigated contained fairly consistent amounts of these two fission products. In one area, however, concentrations of strontium-90, strontium-89 and barium-140 were higher than in other areas. The authors were unable to suggest an explanation for these differences and emphasize the need for further monitoring in order to secure a more exact understanding of the problems involved.

Multiple Antigen against Poliomyelitis, Diphtheria, Pertussis and Tetanus.

C. D. BARRETT *et alii* (*Amer. J. publ. Hlth*, May, 1959) report the results of primary immunization followed by a booster dose 18 months later with a mixed antigen in infants and young children. The antigen contained poliomyelitis and pertussis vaccines combined with diphtheria and tetanus toxoids and satisfactory response to all antigen components was produced in a group of children ranging in age from two months to five years. Children six months of age and older at the time of their initial dose were given a primary course of three monthly inoculations; the younger infants received four doses at monthly intervals. A booster dose of the quadruple vaccine was given about 18 months later. The fourth dose given to the younger infants improved their sero-immunological status and brought their antibody levels into line with those obtained in older children with only three doses. The booster dose of this multiple vaccine was effective in enhancing the sero-immunological status of the children to all antigens in the vaccine. This uniformly high response to the booster dose occurred regardless of the age at which primary immunization was begun and regardless of the antibody level after the primary series. No clinical reactions of any serious consequence were reported or observed.

Alcohol in Road Accidents.

W. HADDON, JR., AND V. A. BRADESS (*J. Amer. med. Ass.*, April 4, 1959) report the results of post-mortem determinations of blood alcohol level in 83 cases in which the driver was killed in an accident involving neither another vehicle nor a pedestrian. These results were collected over a period of eight years in a suburban county. It was found that in 41 cases the blood alcohol level was over 0·15%, while in 17 others it lay between 0·05% and 0·15%. The authors conclude from this and from previous studies that in their area alcohol was a causative factor in the deaths of one-half or more of the drivers killed in such accidents.

An Outbreak of Asian-Strain Influenza in a Closed Population.

R. STALLONES AND E. LENNETTE (*Amer. J. publ. Hlth*, May, 1959) report the results of a full investigation of a severe outbreak of respiratory disease, attributable by laboratory tests to Asian-strain influenza virus, which occurred at a hospital for mentally retarded persons in October, 1957. There were 1391 cases of influenza, with 15 deaths, out of 2456 resident patients. This gives a clinical attack rate of 57% and a case fatality rate of 10·8 per 1000. Attack rates are shown to vary according to the contact rate of the patients, with those allowed to attend school having the highest rate and those confined to bed the lowest. From the results of examination of sera from a sample of the hospital population, the clinical attack rate understated the total infection rate, which was estimated as between 70% and 80%. The ratio of apparent to subclinical infections was estimated at about 3 : 1.

Socio-Economic Factors in the Distribution of Hepatitis.

G. GOLDSTEIN AND P. WEHRLE (*Amer. J. publ. Hlth*, April, 1959) review the epidemiology of hepatitis in Syracuse, U.S.A., to obtain further data on the relationship of socio-economic status to the prevalence of the disease and to determine the proportion of infective to serum hepatitis. Hospital and Health Department records were used. Epidemiologically and clinically, most of the cases appeared to be ones of infective hepatitis. In only 1·9% of the hospital cases was there a history of administration of blood or blood products within six months of the patient's admission to hospital. A

striking correlation was observed between socio-economic area in the community and both the frequency and age distribution of the cases. Higher total case rates and higher rates among children were observed in the lower socio-economic groups, while the adults in these categories had lower rates of clinical hepatitis in spite of heavier community and family exposure. The authors suggest that the prevalence of this infection may be favoured by factors such as crowding and the poorer hygiene and sanitation often found in the lower socio-economic groups. These factors may result in more frequent infection of children with a resultant greater immunity of adults in these circumstances.

Sanitary Accommodation on Building Sites.

W. THOMPSON AND J. BROWN (*Med. Offr, April 10, 1959*) report the results of an inquiry into standards of sanitary accommodation provided for workmen on 45 building sites registered with the local authority in the Central Division of Glasgow. Although regulations only require that closets shall be "sufficient and suitable", the number provided at each site inspected conformed to requirements for factories with equivalent numbers of employees. On 35 sites, water closets connected to public sewers were provided. On seven sites there were chemical closets which were emptied twice a week by the local authority. On one site a bucket was provided and emptied as required into a hole dug in an adjacent field, and on another site the sanitary accommodation was a hole in the ground. On only three sites was the accommodation provided considered "dirty". No attempt was made to control flies, and faecal material was usually exposed to flies where water closets were not provided. The authors consider that their investigation indicated a need for improved sanitary facilities for workers in the building industry from an amenities rather than a public health point of view. They suggest legislation to provide for a definite number of conveniences with a definite standard of comfort and privacy.

PHYSICAL MEDICINE AND REHABILITATION.

Oral Intermittent Positive Pressure Breathing in Poliomyelitis.

W. D. LOESER AND M. F. KERR (*Arch. phys. Med.*, May, 1959) describe a new method of administering intermittent positive pressure breathing, in which filtered room air is intermittently pumped to the patient's mouth through a hose and pipe-stem mouthpiece. Pressure is provided by a cuirass pump. The authors state that oral intermittent positive pressure breathing (OIPPB) has proved a practical method of artificial ventilation for convalescent poliomyelitis patients. Patients can regulate the intake of air in two ways—by closing or opening the soft palate as a valve, and by permitting escape of excess air at the mouth. OIPPB has several advantages over other methods of artificial ventilation. It allows self-regulation of tidal volume by the patient. It permits partial self-regulation of rate. It simplifies care, because of better access to the patient. It frees the patient from the encumbrance of a shell or tank. It permits standing or walking when possible. It maintains mobility of the thoracic cage. The authors discuss the limitations of the method, and state that proper training is necessary; eating is difficult, and dryness of the mouth may occur. The method, like other methods embodying the principle of positive pressure, may affect the peripheral circulation. Effects noted are elevation of intrapleural and right atrial pressure, reduction of venous return, peripheral vasoconstriction, and increased venous pressure. However, these circulatory changes are minimal when expiration takes place against ambient pressure and expiratory time exceeds or at least equals inspiratory time. Even severaly paralysed patients are able to tolerate eight hours' use of the method per day. The method proved useful for 34 of 53 poliomyelitis patients who required mechanically controlled ventilation. Two cases are reported.

Extended Sympathetic Denervation in Chronic Arthritis.

R. HERFORT AND S. H. NICKERSON (*Arch. phys. Med.*, April, 1959) state that pain arising in the weight-bearing joints is the major source of disability in most cases of chronic arthritis. The difficulty of permanently and consistently alleviating joint pain is the principal obstacle to the rehabilitation of these patients. During the past three and a half years the authors have employed a surgical technique of so-called extended lumbar sympathectomy on a group of some 15 unselected patients with advanced rheumatoid arthritis and osteoarthritis of the hip and/or knee joint, and in an addendum to their paper they state that the series has been increased by another 14 similar patients. The operative procedure consists of an ipsilateral retroperitoneal lumbar sympathetic denervation encompassing the lumbar sympathetic trunk distal to the crus of the diaphragm, accessory sympathetic ganglia and decussating fibres in the prevertebral lumbar plexus. All the patients were middle-aged or elderly, and the procedure had no associated morbidity or mortality. In the immediate post-operative period the patients experienced remarkably effective, consistent and lasting relief of joint pain, with concomitant improvement in joint mobility and in general functional capacity. The first group of 15 patients has now been followed up for periods up to four years after operation, and in all instances the relief of joint pain and the improvement in mobility have persisted. No untoward effects have been noted in the follow-up period. Charcot arthropathy has not occurred, nor is it expected to occur.

Iontophoresis Studies with a Radioactive Tracer.

H. T. ZANKEL, R. H. CRESS AND H. KAMIN (*Arch. phys. Med.*, May, 1959) have carried out studies, using radioactive iodine as iodide ion and a galvanic current, to determine the amount of iodine absorbed through the skin and into the circulation, as manifested by its recovery from the urine. Iodine was applied to the skin for 30 minutes, with and without heat, moist packs and iontophoresis. With iontophoresis, about 6% of the iodine applied was absorbed; previous treatment with heat did not significantly alter this figure. In the absence of current, with or without heat, less than 0·25% was absorbed. The work is being continued.

Effects of Ultrasound on Growing Bone

J. L. VAUGHEN AND L. F. BENDER (*Arch. phys. Med.*, April, 1959) have investigated the effects of ultrasound on growing bone. The experimental animals were 20 rabbits, which were treated daily with ultrasound in a dosage of one watt per square centimetre. The left upper epiphyseal area was treated from the age of three months until X-ray evidence of epiphyseal closure was obtained (age six to eight months). The animals were then sacrificed, the tibial and humeral bone length was measured, and material from the epiphyseal area was examined histologically. The authors conclude from their study that, in rabbits, ultrasound applied in the manner and dosage stated has no significant effect on bone length, epiphyseal integrity or epiphyseal closure time.

Ultrasound and Temperature Rise in Tissues.

J. W. GERSTEN (*Arch. phys. Med.*, May, 1959) has studied the temperature rise in various tissues in the dog on exposure to ultrasound. Various areas of the anæsthetized animal were sounded at frequencies of 490 kc. per second, 1 mc. per second, and 3 mc. per second. In all situations tested the effective depth of penetration at 3 mc. per second was not great, as measured by temperature rise. In relatively superficial bone the temperature rise at the bone surface was greater than that in overlying muscle at frequencies of 490 kc. and 1 mc. per second. At the two lower frequencies studied, the temperature rise within the spinal canal was approximately the same as that in subcutaneous tissue. "Selective" heating of nerve was especially evident at 490 kc. per second.

Rehabilitation after Cerebral Vascular Accidents.

M. LOWENTHAL, J. S. TOBIS AND I. R. HOWARD (*Arch. phys. Med.*, May, 1959) present the results of the first year of study of 232 cases of cerebral vascular accident in the department of physical medicine and rehabilitation of the New York Medical College-Metropolitan Medical Center, from the point of view of rehabilitation and prognosis. They state that 42% of the patients died, most of them within two weeks. Of the surviving group, approximately 36% were discharged within two weeks, and about 75% of those who remained beyond two weeks received some rehabilitation care. Assessment of the condition upon discharge of the surviving patients showed that 65% either were independent or required only slight assistance, 32% required moderate assistance, and 3% required a great deal of assistance and were considered severely disabled.

Brush Up Your Medicine.

STEROID HORMONES: II. SEX HORMONES.

Sex hormones can be classified into three types according to their principal actions: androgens, œstrogens and progestogens. Androgens are substances which promote the development of the sexual organs and secondary sexual characteristics of adult males. Œstrogens are substances which bring about cornification of the vaginal epithelium, like that seen during natural œstrus, when administered to castrated or immature female rats or mice. Pro-œstrogens are substances which are not themselves œstrogenic, but which are converted to œstrogens in the body. Progestogens are substances which share the important actions of progesterone, especially the favourable effect of this substance upon the implantation of the fertilized ovum. Certain substances show some of the actions of more than one type of sex hormone. The naturally occurring mammalian sex hormones are steroids; but a number of synthetic and naturally occurring substances, which are not steroids, possess œstrogenic properties.

Androgens.

In addition to those actions which give them their name, androgens possess the property of promoting protein anabolism. No doubt it will turn out that these two major actions are related, but for therapeutic purposes they may be regarded as distinct. For many years testosterone propionate given by injection and methyl-testosterone given by mouth were the androgenic preparations in common use; the propionate ester of testosterone was used because it proved to have a longer action than the unesterified parent compound. However, within recent years two changes have been sought in the original hormone—namely, longer action on the one hand and enhanced protein anabolic properties, developed at the expense of androgenic activity, on the other hand. Among the preparations designed to answer the first requirement, two types have emerged. Firstly, the hormone can be esterified in various ways—e.g., testosterone cyclopentylpropionate, testosterone œnanthate and testosterone hexahydrobenzoate. Of these substances, testosterone cyclopentylpropionate has been most widely used. Secondly, the hormone can be suspended or dissolved in an oily or other medium such as to delay release of the hormone, or microcrystals can be used in watery solutions. Certain limitations are set upon these procedures—e.g., esterification can eventually proceed to a point where the androgenic properties are lost, and oily solutions are restricted by undesirable properties of the injected oil.

The search for a hormone showing maximal anabolic activity and minimal virilizing effects has been long and not altogether successful. Methyl androstenediol and 17-ethyl-17-hydroxy-19nor-androst-4-en-5-one, called "Nilevar", are among the preparations developed with this end in view. Reports so far are conflicting, and the success of these preparations in the hands of certain workers has not altogether been confirmed. It is intended that these preparations shall be helpful in speeding the recovery of patients suffering from reversible or curable wasting diseases. The most promising reports concern the substance 9-fluoro-11-hydroxy-17-methyl testosterone ("Halotestin"), which has been used in advanced mammary carcinoma; in this condition it has produced remissions in patients suffering from metastases in bone and occasionally from soft-tissue metastases, without causing virilization.

Uses as Androgens.

Substitution Therapy.—In patients suffering from prepubertal testicular failure, androgens will bring about the development of normal secondary sexual characteristics. This response, which has been described as little short of miraculous, is accompanied by the development of a confident, mature personality. In cases of adult castration or hypogonadism, androgens are capable of maintaining normal sexual development. The treatment of choice consists of either of one of the long-acting androgenic preparations for intramuscular administration given monthly, or an implantation of six 100 mg. pellets of testosterone every six months. The dosage and frequency of treatment require adjustment in individual cases.

The Male Climacteric.—When symptoms suggestive of a male climacteric are encountered in late middle life, androgen therapy is worthy of trial, (e.g., methyl testosterone, 25 mg. daily). Preparations for oral use are useful in the first instance, and in the event of a satisfactory response, long-acting preparations can be substituted (e.g., testosterone propionate in oil, 50 mg. every four weeks).

Functional Menorrhagia.—When menstrual bleeding is regular and follows ovulation but is excessive, treatment with androgens is useful—e.g., methyl testosterone, 10 mg. per day for two months. Treatment should not be continued for longer than two months without an interval of one month before the next course is begun. This treatment should, whenever possible, be avoided at puberty.

Hormonal Mastopathy.—The non-committal name given to this condition indicates the limitations of present-day knowledge of the subject. The condition of painful breasts in adult women, occurring just before menstruation, often responds to oral administration of androgens in the same dosage as that used in menorrhagia.

Carcinoma of the Breast.—In selected cases, large doses of androgens may favourably influence the course of carcinoma of the breast.

Frigidity.—Small doses of androgen (e.g., methyl testosterone, 5 mg.) stimulate female libido; but underlying psychological conflicts may make this form of treatment useless or even undesirable.

Senile Pruritus.—This often responds to androgen therapy (e.g., methyl testosterone, 25 mg. per day).

Miscellaneous Uses.—In addition to these relatively well-defined indications, androgens are used in many conditions for which no rationale can be offered. In such cases the use of these hormones is empirical and results are unpredictable. These conditions include prostatic hypertrophy, psychogenic impotence, nocturnal enuresis, acne, delayed union of fractures and coronary artery disease. It is safe to say that at present the use of androgens in these condition is not justified except in specially selected cases.

Uses as Protein Anabolic Hormones.

Among the host of conditions for which protein anabolic hormones are recommended, the following are especially important: (i) delayed recovery from an acute illness—e.g., poliomyelitis, virus pneumonia; (ii) chronic wasting diseases—e.g., tuberculosis and carcinomatosis; (iii) delayed recovery from surgical operations and burns; (iv) protein loss in cases of protein exudates and after hæmorrhage; (v) malnutrition as in anorexia nervosa, or conditioned malnutrition in diseases of the bowel—e.g., steatorrhœa and chronic diarrhœa. As mentioned earlier, the value of this form of therapy still remains to be established, especially in the case of the newer non-virilizing preparations.

Side-Effects and Contraindications.

The principal side-effects of androgens include hirsutism and other androgenic manifestations in women. The chief contraindications are carcinoma of the prostate and liver cell damage.

Œstrogens.

The synthesis of stilbœstrol provided endocrinologists with a potent, cheap œstrogen which could be taken by mouth. With such a convenient preparation, the search for more satisfactory œstrogens was less urgent than in the case of other hormones. However, three improvements in the properties of stilbœstrol have been sought: (i) absence of nausea, (ii) longer action, (iii) pituitary stimulation.

The search for preparations free from nauseating effects was directed at imitating and modifying the natural hormones, and four useful œstrogens are available for patients in whom stilbœstrol causes nausea: (*a*) ethinyl œstradiol, (*b*) equine conjugated œstrogen ("Premarin"), (*c*) sodium œstrone sulphate, (*d*) piperazine œsterone sulphate. These preparations can be used locally as ointments (for acne) and intravenously as an emergency measure in uterine hæmostasis. For most purposes, equine conjugated œstrogen is a convenient preparation.

Long-acting œstrogens have recently been developed along three lines: (i) esterification, (ii) crystalline aqueous suspension, (iii) fat-soluble pro-œstrogens. Various esters maintain the desirable œstrogenic properties while prolonging the duration of action. These include: (*a*) œstradiol propionate, (*b*) œstradiol valerianate, (*c*) œstradiol undecylate. Crystalline aqueous suspensions also lengthen the duration of action of œstrogens, while the unique tri-p-anisylchloroethylene ("Tace") is a fat-soluble pro-œstrogen which is slowly released from the fat depots and converted in the liver to œstrogenic substances. Long-acting preparations are useful in the management of malignant disease (chiefly in carcinoma of the prostate), and are preferred

by some workers in the treatment of the menopause. However, for most purposes œstrogens of short action given orally are useful.

Pituitary stimulation represents a very special use of œstrogens, and it is too early to discuss the value of such stimulation and the possibility of its production by current hormones. The monobenzyl ether of stilbœstrol has proved useful in the treatment of secondary amenorrhœa and infertility in selected cases. It is hoped that at appropriate levels of dosage, this substance may promote the release of pituitary gonadotrophins without being œstrogenic in any of the usual ways.

TABLE I.
Androgens.

Chemical Name.	Proprietary Name.	Preparation.	Available Strengths.
Testosterone ..	"Testoviron."	Implant.	100 mg.
	Testosterone(B.D.H.)	Implant.	25, 50, 100 mg.
	"Perandren."	Implant.	100 mg.
	"Virormon."	Implant.	100, 250 mg.
Testosterone propionate in oil.	"Neo-Hombreol."	Ampoules.	5, 10, 25, 50 mg.
	"Perandren."	Ampoules.	5, 10, 25, 50, 100 mg.
	"Sterandryl."	Ampoules.	10, 25, 50, 100 mg.
	"Testoviron."	Ampoules.	10, 25, 50, 100 mg.
	——	Ampoules.	5, 10, 25, 50, 100 mg.
Testosterone propionate implant.	——	Implant.	100 mg.
	"Sterandryl."	Implant.	100 mg.
Testosterone propionate aqueous suspension.	"Testaform."	Ampoules.	5, 10, 25, 50 mg.
Testosterone phenylpropionate.	"Testaform P.P."	Ampoules.	10, 50 mg.
Testosterone œnanthate.	"Primoteston Depot."	Ampoules.	250 mg.
Testosterone œnanthate with testosterone propionate.	"Primoteston Depot."	Ampoules.	50, 100 mg.
Testosterone mixed esters.	"Sustanon."	Ampoules.	100, 250 mg.
Methyl testosterone	"Glosso-sterandyl."	Linguets.	5, 10, 25, 50 mg.
	"Perandren."	Linguets.	5, 10, 25, 50 mg.
	"Sublings."	Linguets.	5, 10, 25, 50 mg.
Anabolic androgens:			
17-ethylhydroxy-19-nor-androsterone.	"Nilevar."	Tablets.	10 mg.
		Ampoules.	25 mg.
19-nor-testosterone phenylpropionate.	"Durabolin."	Ampoules.	25 mg.
9-fluoro-11-hydroxy-17-methyl testosterone.	"Halotestin."	Ampoules.	25 mg.
Methyl androstenediol.	"Protandren."	Tablets.	10, 25, 50 mg.
	"Stenediol."	Tablets.	10, 50 mg.

Uses of Œstrogens.

Menopause.—It is no longer believed that every woman reaching the menopause requires immediate and prolonged œstrogen therapy. Today fewer women are treated with œstrogens for menopausal symptoms, doses are smaller (0·3 mg. of stilbœstrol per day or its equivalent), and therapy is not maintained indefinitely. Œstrogens are given in courses lasting four to six weeks, with intervals of one or two weeks, in order to guard against uterine hæmorrhage. Androgens are used together with œstrogens, and in numerous preparations the two hormones are combined in tablet or injectable form; however, such preparations have certain disadvantages. The response of women to androgens shows great individual variation, and if pharmacological doses of the androgenic component are to be used without causing virilization, the dose must be adjusted independently of that of the œstrogen. Androgens are believed to maintain protein anabolism, to induce a sense of well-being and to sharpen the libido. Similar combinations of androgens and œstrogens are used in larger doses for menopausal osteoporosis, and again the two hormones should be dispensed separately.

Hæmostasis.—When menorrhagia becomes excessive and prolonged, it can be promptly and effectively arrested by large doses of œstrogen—e.g. 0·2 mg. of ethinyl œstradiol by mouth every second waking hour, or 20 mg. intravenously every six or 12 hours for four doses.

Dysmenorrhœa.—When dysmenorrhœa secondary to pelvic lesions is excluded, it is possible to define a condition of true spasmodic dysmenorrhœa; this condition does not occur in the absence of ovulation, and œstrogens present a convenient way of suppressing ovulation and hence of producing painless withdrawal bleeding. Stilbœstrol is given in doses of 2 mg. per day (or equine conjugated œstrogens in doses of 5 mg.) for 14 days, beginning within the first five days of the menstrual cycle. Each course is followed by another, with at least one week's interval between.

Substitution Therapy.—The rare condition of gonadal agenesis (Turner's syndrome) is generally treated by means of œstrogens, which are administered in courses of 21 days, each of which is followed by withdrawal bleeding. Treatment should not be commenced until epiphyses have fused.

Miscellaneous Uses.—Œstrogens are used in the treatment of acne, carcinoma of the prostate, endometriosis and suppression of ovulation (as in the case of dysmenorrhœa), and are useful in the management of bucco-vulval ulcers. The use of œstrogens to suppress lactation is now widespread, while attempts to limit the growth of tall girls by fusing the epiphyses with the aid of these hormones is reserved for specially selected patients.

Progestogens.

Although active preparations of the hormone of the corpus luteum have been available for many years, progesterone has proved a disappointment as a therapeutic weapon. In spite of claims that the hormone is effective in the treatment of recurrent abortion and of certain types of infertility, most workers have remained sceptical of these claims. Chemical and pharmacological modifications of the original hormone have, therefore, not appeared in the profusion seen in the case of androgenic and œstrogenic preparations. Inevitably a progestogen which could be taken by mouth was sought, and ethisterone was soon produced; but this substance found only a limited place in endocrinology. More recent preparations include norethisterone, methylnorethisterone, methylnortestosterone and 17α-hydroxyprogesterone caproate. These preparations are more potent than ethisterone, and are effective when taken orally.

As with other steroids, long-acting injectable preparations have been sought, and both microcrystals and oily suspensions have been used with success. Chemists working with progesterone have not enjoyed the presence of a hydroxy group which could be esterified, and it was not until recently that it became known that although 17-hydroxyprogesterone shows no progestational action, esterification by acetic or caproic acid produces strong progestational activity.

TABLE II.
Œstrogens.

Chemical Name.	Proprietary Name.	Preparation.	Available Strengths.
Ethinyl œstradiol	"Estigyn."	Tablets.	0·01, 0·02, 0·05, 1·0 mg.
	"Ethidol."	Tablets.	0·01, 0·05, 0·1, 1·0 mg.
	"Eticyclin."	Tablets.	0·01, 0·05, 1·0 mg.
	"Lynoral."	Tablets.	0·01, 0·02, 0·05, 0·1, 1·0 mg.
	"Primogyn C."	Tablets.	0·02, 0·05 mg.
	"Primogyn M."	Tablets.	0·2 mg.
Œstradiol valerianate	"Primogyn-Depot."	Ampoules.	10 mg. per millilitre.
Conjugated equine œstrogens.	"Premarin."	Tablets.	0·625 and 1·25 mg.
Trianisylchloroethylene.	"Tace."	Capsules.	12 mg.
Œstradiol monobenzoate.	"Œstroform."	Ampoules.	1, 2, 5 mg.
	"Dimenformon."	Ampoules.	1, 5, 10 mg.
	"Progynon B. Oleosum."	Ampoules.	1, 5 mg.
	"Ovocyclin."	Ampoules.	0·1 mg.

Uses.

In spite of its unpromising introduction into the pharmacopœia, progesterone and its derivatives now enjoy some (though limited) success.

Progesterone Withdrawal Bleeding.—It seems likely that natural menstrual bleeding results from withdrawal of œstrogen and progesterone from the blood-stream. When the endometrium is primed by œstrogen, progesterone will lead to withdrawal bleeding a few days after this drug is withheld. Either 25 mg. of progesterone given daily by intramuscular injection for four days or 50 mg. of ethisterone given daily by mouth, for ten days, can be used. Bleeding usually occurs two or three days after each course and resembles a natural menstrual period. This treatment is indicated for three conditions: (i) metropathia hæmorrhagica; (ii) amenorrhœa: secondary amenorrhœa of recent origin with anovulatory cycles can occasionally be made to revert to normal menstrual cycles by progesterone therapy; (iii) infertility, in which an attempt is made to induce normal pituitary function by imitating normal menstrual cycles. In the second and third conditions, vaginal smears provide a useful index of adequate œstrogenic priming; without such priming progesterone by itself is ineffective.

Luteal Failure.—When "infertility" results, not from failure of fertilization, but from failure of implantation of the fertilized ovum, the fault can occasionally be traced to inadequate secretion of progesterone by the corpus luteum. Evidence for this failure can be obtained by studying urinary pregnanediol excretion, and by demonstrating that the interval between ovulation and the onset of menstruation is less than eleven days. Progesterone sometimes corrects this abnormality.

TABLE III.

Progestogens.

Chemical Name.	Proprietary Name.	Preparation.	Available Strengths.
Ethisterone ..	"Ethisterone."	Tablets.	5, 10, 25 mg.
	"Lutocyclin."	Tablets.	5, 10, 25 mg.
	"Oraluton."	Tablets.	5, 10, 25 mg.
	"Progestoral."	Tablets.	5, 10, 25 mg.
	"Proluton C."	Tablets.	5, 10, 25 mg.
Nor-ethisterone ..	"Primolut N."	Tablets.	5 mg.
	"Noriutin."	Tablets.	5 mg.
Progesterone ..	"Progestin."	Ampoules.	2, 5, 10, 25 mg.
	"Lutocyclin."	Ampoules.	2, 5, 10, 25, 50 mg.
	"Progestin I.V."	Ampoules (intravenous).	20 mg.
17-α-hydroxyprogesterone caproate.	"Proluton-Depot."	Ampoules.	65, 125, 250 mg.

Habitual Abortion.—In spite of disappointing results in the past, recent studies suggest that newer progestogens may prove helpful in the management of habitual abortion. However, a warning is necessary in view of possible androgenic and other effects upon the fœtus, and the proof that progestogens are of value in this condition must be beyond reproach before most endocrinologists will be prepared to use these hormones.

Post-partum Psychosis.—As in premenstrual tension, so in post-partum psychosis, progesterone has been tried as an empirical measure with some possible success, although assessment of such claims is still an open question.

Sydney. PETER HALL.

Correspondence.

WHAT MADE THE CLOCK TICK?

SIR: I was fascinated by the very interesting article of W. A. Osborne, which you so wisely printed in the Journal dated July 4, on page 26. The science of gimletology has been sadly neglected in our present-day quaternary education. This writer formulated the following interesting hypothesis: "The objection that gimlets are not seen when the works are exposed is easily explained by the hypothesis that there is a gaseous precursor, gimletogen, which is acted upon by a gaseous horozyme." This statement is only partially correct, as a state of disequalibrium ensues, wherein the gaseous precursor, "gimletogen", is rapidly deoxofluorized before it is actually formed, and the gaseous horozyme is then liquified and disappears in the characteristic oxoplasmic blue flame.

Yours, etc.,

S. G. (BUL) ROWE, D.Sc. (Oxom.), G.O.P.R.H.,
Past President, Oxometrical Society, Sydney.

Broughton Hall Psychiatric Clinic,
Leichhardt, N.S.W.
July 3, 1959.

SIR: I noted, with some interest and considerable alarm, in your issue of July 4, 1959, at page 26, some notes under the title "On The Periphery". "What made the Clock Tick?". My alarm was occasioned by the exclusively horochemical approach to the study of the observed facts.

Whilst it is distinctly possible—and even likely—that the facts of horopathology may ultimately be found to rest on disturbances in horozyme systems, the evidence which has come out of synthetically-orientated individual and group horotherapy makes it clear that, for the present at least, our explanations are best couched in the terms of horosynthesis. However, it must also be agreed that recent work on the temporal lobe (*tempus fugit* and all that jazz) must have some applicability to horology.

The facts set forth by Dr. Osborne (*loco citato*) form a striking example of the great damage that can be done by the attempted use of horoanalytical techniques by those unskilled in their use. It may well be true that horoanalysis is frequently a necessary preliminary to horosynthesis, but dabbling in the former by amateurs is likely to produce a disruption of the horologic homœostasis.

It would be well, I think, for the horo-biochemists to recall the liticko theory of clock development and behaviour (with emphasis on the importance of six o'clock—Latin *sex*), in which it is made clear that the ick is the source of all horic energy, representing, as it does, the basic drives within all clocks. The ick makes contact with the world of external reality only through the shego, and a regulating mechanism known as the supershenogo gradually develops.

It has become clear that no clock can be considered as an isolate. A clock has meaning only in relation to other clocks and to time, generally. Hence the development of the theory of the "spatial unconscious" which still has some adherents.

It is hoped that this communication will serve to clarify the nature of the contributions which horo-synthetic theory can make to the answering of Dr. Osborne's original question: "What made the clock tick?"

Yours, etc.,

W. B. GRANT,
Medical Officer.

Broughton Hall Psychiatric Clinic,
Leichhardt, N.S.W.
July 20, 1959.

FAVISM IN ASIA.

SIR: Several reports of cases of favism have appeared in Australia recently (Harley and Dods, 1957; Brooks, James and Stubber, 1958; Moore, 1958). The subjects in every case were of Mediterranean origin (Greek or Italian). Favism is common in the Mediterranean region.

Until quite recently, this hereditary predisposition to hæmolytic episodes after the ingestion of the beans, or inhalation of the pollen from the flowers, of *Vicia faba* was considered to be specific to the peoples of the Mediterranean region. The same was true of Cooley's anæmia (Mediterranean anæmia, thalasssemia). In both cases, however, this position has proved to be untenable. Several reports of favism in Chinese subjects have recently been made (Du, 1952; Wang and Wang, 1956; Chu, Ni and Yang, 1956; Pu, 1957). Chang (1959) has made a clinical analysis of 228 cases, and Bernard (1959), reporting on "Blood Diseases in China", stated that "Favism is responsible for severe hæmolytic anæmias with hæmoglobinuria in many regions of China, mostly around Hang-Chow".

The defect in the erythrocytes which somehow predisposes them to rapid hæmolysis after ingestion of fava

beans is a hereditary deficiency in the enzyme glucose-6-phosphate dehydrogenase (Sansone and Segni, 1958; Szeinberg, Sheba and Adam, 1958). The same defect is responsible for susceptibility to drug-induced hæmolysis (Carson, Flanagan, Ickes and Alving, 1956). In fact, it has been shown that a hæmolytic episode may be provoked by administration of primaquine or other drugs in subjects predisposed to favism, or who have actually had hæmolytic episodes following fava beans (Larizza, Brunetti, Grignani, and Ventura, 1958).

The mechanism of the hæmolytic reaction in susceptible individuals is not clear. Fegler (1952) suggested that a certain amount of reduced glutathione is important in maintaining the integrity of structure of the erythrocyte. We have recently carried out experiments using human, monkey, ox and horse bloods, in which the rate of spontaneous hæmolysis was measured in samples treated with an isotonic solution of sodium nitrite and in untreated aliquots. The effect of sodium nitrite on erythrocytes is to oxidize all the contained reduced glutathione, to convert the oxyhæmoglobin to methæmoglobin and at the same time denature the globin component of the methæmoglobin so formed. No differences in the rates of hæmolysis were noted over 24 hours at 37° C. between the treated and untreated erythrocytes (Vella, 1959).

Using a simple method for the detection of deficiency of glucose-6-phosphate dehydrogenase activity devised by Professor A. G. Motulsky and Dr. J. M. Campbell, of the University of Washington, we have found this enzyme defect in 2·22% of 225 Chinese, in 3·26% of 92 Indian and in 40·0% of 15 Jewish male blood donors. No enzyme deficiency was found in 76 European "whites" and in 126 Malays—all male blood donors. When umbilical cord blood samples were studied, the defect was found in 2·63% of 76 male Chinese samples, but was not found in 67 female Chinese, 13 male and 10 female Indian samples. Amongst 83 blood samples from patients with anæmia, mainly hæmolytic in nature, of all ages, 10 were enzyme deficient and of these eight were Chinese and two were Jews. One of the Chinese and one of the Jews with the enzyme defect were hospitalized for jaundice and hæmoglobinuria after the taking of drugs, while four of the enzyme-deficient Chinese were infants suffering from or just recovering from neo-natal jaundice.

The enzyme defect was not related to the type of hæmoglobin contained in the erythrocytes. Thus, all the blood samples referred to above contained only normal hæmoglobin (A in the adult samples, and A + F in umbilical cord samples and those from infants); and erythrocytes containing a variety of abnormal hæmoglobins (A + E, E + E, E + F, A + L, A + H, and umbilical cord samples containing abnormal "fast" or "slow" fœtal hæmoglobins) or obtained from subjects with thalassæmia major or thalassæmia minor, only occasionally showed the enzyme defect.

The Jews, amongst whom the defect was detected in 40% of an admittedly small sample, were Sephardic Jews who originated from Iraq and Persia. Szeinberg and Sheba (1958) found an incidence of 20% for the enzyme deficiency amongst Jews of similar origins living in Israel.

The drugs which have been reported to induce hæmolysis in susceptible subjects include: primaquine, acetanilide, phenacetin, nitrofurantoin, para-aminosalicylate, "Promizole" and several sulphonamides. There is little doubt that more cases of favism or drug induced hæmolysis will be detected if it is remembered that susceptibility is not restricted to people of Mediterranean origin.

Yours, etc.

T. VELLA,
M.Sc., M.D., M.A. (Oxon.), A.R.I.C. (London).
Department of Biochemistry,
University of Malaya in Singapore,
Singapore.
July 14, 1959.

References.

BERNARD, J. (1959), "Blood Diseases in China", *Blood*, 14: 605.

BROOKS, E. A. V., JAMES, G. A., and STUBBER, L. A. (1958), "Favism in Western Australia", MED. J. AUST., 2: 455.

CARSON, P. E., FLANAGAN, C. L., ICKES, C. E., and ALVING, A. S. (1956), "Enzymatic Deficiency in Primaquine-Sensitive Erythrocytes", *Science*, 124: 484.

CHANG HSIAO-HSIANG (1959), "Favism. Clinical Analysis of 228 Cases", *Chin. J. Pediat.*, 10: 63.

CHU CHANG-LIANG, NI YANG CHENG and YANG SSU-YUAN (1956), "Favism in Shanghai. Report of Two Cases", *Chin. J. Pediat.*, 7: 137.

FEGLER, G. 1952), "Relationship between Reduced Glutathione Content and Spontaneous Hæmolysis in Shed Blood", *Nature*, 170: 624.

HARLEY, J. D., and DODS, L. (1957), "Hæmolysis Following the Ingestion of Uncooked Broad Beans", MED. J. AUST., 2: 561.

LARIZZA, P., BRUNETTI, P., GRIGNANI, K., and VENTURA, S. (1958), *"L'individualità bio-enzimatica dell'eritrocito fabico; sopra alcune anomalie biochimiche ed enzimatiche delle emazie nei pazienti affetti da favismo e nei loro familiari"*, *Minerva med. (Torino)*, 49: 3769.

MOORE, H. S. (1958), "A Suspected Case of Favism", MED. J. AUST., 2: 733.

PU SHAO-MING (1957), "Favism in Peking. Report of a Case and Review of Literature", *Chin. J. intern. Med.*, 5: 902.

SANSONE, G., and SEGNI, G. (1958), *"Nuovi aspetti dell-alterato biochimismo degli eritrociti difavici: assenza pressoche completa della glucose-6-P dei-drogenasi"*, *Boll. Soc. ital. Biol. sper.*, 34: 327.

SWUN-DEH DU (1952), "Favism in West China", *Chin. med. J.*, 70: 17.

SZEINBERG, A., and SHEBA, C. (1958), "Hæmolytic Trait in Oriental Jews Connected with an Hereditary Enzymatic Abnormality of Erythrocytes", *Israel med. J.*, 17: 158.

SZEINBERG, A., SHEBA, C., and ADAM, A. (1958), "Enzymatic Abnormality in Erythrocytes of a Population Sensitive to Vicia Faba or Hæmolytic Anæmia Induced by Drugs", *Nature*, 181: 1256.

VELLA, F. (1959), "Observations on Spontaneous Hæmolysis in Shed Blood", *Experientia (Basel)*, in the press.

VELLA, F. (1959), "Susceptibility to Drug Induced Hæmolysis in Singapore", *Med. J. Malaya*, in the press.

VELLA, F., and PHOON WAI-ON (1959), "Hæmolytic Jaundice in a Drug Sensitive Patient in Singapore", *Med. J. Malaya*, in the press.

WANG CH'I and WANG CH'UNG-FANG (1956), "Favism in Children in Kueiyang: Report of Four Cases", *Chin. J. Pediat.*, 7: 139.

LONG-ACTING PROGESTERONE PREPARATIONS AND ORALLY ADMINISTERED "PRIMOLUT N" IN THE TREATMENT OF HABITUAL ABORTION.

SIR: In reply to the inquiry of R. P. Shearman re duration of the effect of "Proluton Depot". One such reference is: Davis, M. E., and Weld, G. L., 1955, *Journal of Clinical Endocrinology and Metabolism*, 15: 929. They state: "The action of 17-hydroxy-progesterone-17-capronate was definitely prolonged: uterine bleeding from a secretory endometrium occurred 14 to 19 days after administration."

Yours, etc.

12 Collins Street, W. J. RAWLINGS.
Melbourne.
Undated.

FITNESS OF DRIVERS OF PUBLIC SERVICE VEHICLES.

SIR: In an ex-cathedra statement printed in your issue of July 4, The Royal Australasian College of Physicians lists recommendations on the fitness of drivers of public service vehicles. Among those dealing with hypertension is:

> 4. Persons found to have blood pressures above average normal figures for their age at examination prior to employment as drivers of public service vehicles should not be employed as drivers.

What is intended by the word "normal" is not clear; but it follows from the definition of "average" that about half the persons examined will have blood pressures above the average for their age and would therefore fail to meet the standard quoted above.

I do not suppose that the College is wittingly advocating a medical standard which, if followed, would inevitably lead to the rejection of half the applicants. Perhaps for this reason, the following paragraph, 5, appears to qualify paragraph 4. Paragraph 5 suggests, as maximum acceptable values for new entrants, 140/90 "up to 40 years of age" and 150/94 "at 50 years of age". These values do not look like the population averages called up by paragraph 4. As a quick check, they may be compared with the data of Master for United States males.[1] Each of the four values is not close to the mean of the appropriate distribution, but is nearly equal to the mean plus one standard deviation.

The effect of applying even the modified limits of paragraph 5 may be estimated by examining the blood-pressure distributions of a group of "drivers of public service vehicles", a group that may well have relatively good health—namely, Australian airline pilots. One or both of

[1] Master, A. M., Garfield, C. I., and Walter, M. B. (1952), "Normal Blood Pressure and Hypertension", Lea and Febiger, Philadelphia.

the figures 140/90 are exceeded by 8·9% of pilots up to age 40, and 150/94 by 7·5% above age 40.

It is reasonable to expect that, of intending vehicle drivers, percentages of the same order would fail to meet the College's suggested standard. This is a rather large rejection rate from a single item in the medical examination. Moreover, eliminating these percentages would, on Norman's findings cited in the College's statement, lead to a negligible gain in safety.

The recommendations of paragraphs 4 and 5 are not only inconsistent with each other, but also with the preamble to the section on hypertension which says: " . . . it is held that evidence of hypetensive and/or atherosclerotic vascular disease (cerebral, retinal, cardiac or renal) is much more important than the actual levels of blood pressure recorded.'

It would be more in keeping with this last view if it were suggested that public authorities ought, in fact, to be exceedingly cautious about setting up fixed numerical limits for blood pressure beyond which drivers or applicants would have to be disqualified.

Yours, etc.

Department of Civil Aviation, J. C. Lane.
499 Little Collins Street,
Melbourne.
July 13, 1959.

ALCOHOL AS A FACTOR IN MEDICO-LEGAL SUDDEN DEATHS.

Sir: Dr. Hansman's letter verifies Seneca's sarcastic comment *"Non vitae, sed scholae, discimus"*.

I can assure Dr. Hansman that I am well acquainted with the literature on alcoholism, and from a very extensive experience with the treatment of alcoholics, I know how very unsatisfactory it is. And, despite Dr. Hansman's weariness of "extravagant claims", and presumably his hatred of hyperboles, I can assure him that if he is to know alcoholics, he must study them, not from books, of which he is so enamoured, but from life—that is, by mixing up with them constantly. And there are many members of Alcoholics Anonymous who have been sober for many years, some of whom are professional men, who will fully support my argument, which to Dr. Hansman is "as unscientific as it is exaggerated". They alone will give the true clinical facts about their drinking. And if Dr. Hansman is relying on the scientific method, which in alcoholism is dependent to a large extent on what patients tell him, he is relying on a broken reed. For his beloved textbooks will tell him that alcoholics are liars; yet they then proceed to describe alcoholism on what patients have said, surely a masterpiece of successful lying and deceit.

It may also interest Dr. Hansman to know that studies of alcoholism have been based on the population of large cities, mostly in the Old World, on a conforming, inactive population. From such an atmosphere, even from that of Sydney and Melbourne, the true alcoholics, if at all possible, flee to the remote outback, where, by the grace of God, they are beyond the ambit of psychiatric studies and scientific methods. And again it may also interest Dr. Hansman to know that many such, on many days, may drink a bottle of brandy before breakfast, without showing any apparent signs of being under the influence of alcohol. On other days, a glass of brandy will make them very drunk. Why, I do not know.

My statements were made from life, not from books. Only this way can one learn the true facts about alcoholism.

Yours, etc.

Bleahki House, S. J. Minogue.
61 Hunter Street,
Sydney.
July 12, 1959.

TOBACCO SMOKING AND LUNG CANCER.

Sir: Medical science has to its credit many great victories over disease, but its most resounding defeat in this twentieth century has been its failure to convince society that cigarette smoking causes lung cancer. Despite lamentations, exhortations, intense publicity, authoritative statements, statistical pogroms and frightening propaganda, the community remains indifferent. Tobacco is still grown and its consumption is increasing. To many scientists, tobacco is the Fifth Horseman of the Apocalypse—to society it is a necessary balm for the troubled spirit.

Science has based its contentions on statistics, and used this honoured and ancient scientific method in an effort to show a causal relationship—a role for which statistics were never intended. It is not surprising, therefore, as Berkson has recently pointed out, that many unwanted conclusions emanate. The present position is that smoking "causes" quite a number of diseases, and the statistician has an embarrassment of riches. The question now is, what disease is not "caused" by smoking?

Recently to our Research Group, Dr. Rubinstein of the Anti-Tuberculosis Campaign reported (I write from memory) that in his wide and very complete radiographic survey, about 170 cases of lung cancer were detected in New South Wales in over 3,000,000 X-rays. Of these, 30% were in English migrants who constitute less than 10% of the population. The male and female rate was 10:1. Among the affected males the rate in central Sydney was roughly 1:5000, in outer Sydney 1:10,000 and in the country 1:50,000. To avoid lung cancer, therefore, I presume smokers should either live in the country or change their sex. This information, if I report it correctly, strongly supports Percy Stocks' repeated contention that atmospheric pollution is the chief contributing exogenous factor in the avalanche of urban lung cancer in males of European stock.

The statisticians have failed to explain the male predominance, the immunity of many non-European races despite heavy smoking, the diminishing laryngeal cancer rate, the continued tracheal immunity, the lack of correlation between inhalers and lung cancer victims, the American and New Zealand experiences (higher tobacco consumption than in Great Britain accompanies a lower lung cancer rate per million population), and the great difficulty of demonstrating experimentally the entire relationship between tobacco products and carcinogenesis.

Cancer affects a pretty constant segment of the population, and a fall in the incidence of one cancer usually accompanies the rise in another. If scientists could eradicate tobacco from the economy, and if their contention is true that a great fall in lung cancer would ensue, it is interesting to speculate what cancers would then begin to increase. Maybe the community at large would become very expert in the management of colostomy!

I am practically a non-smoker, but am in great sympathy with the comfort and peace which the weed brings to many of my friends. If I wanted to smoke, I feel that no final and incontrovertible evidence has yet been produced by scientists to discourage me—and from smoking anything at that.

Yours, etc.,

Dorchester House, Kenneth W. Starr.
149 Macquarie Street,
Sydney.
July 16, 1959.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

MEDICAL ADVERTISING.[1]

[From the *Australasian Medical Gazette*, July, 1896.]

On Tuesday, 7th July, at a meeting of the Council of the N.S.W. Branch of the British Medical Association, a circular was submitted for consideration from Messrs. Percy and Dearsley with reference to the City Directory, wherein it was proposed that all business premises in each street should be advertised on tablets to be erected in prominent positions. It was pointed out that, in this circular, special stress was laid on the value of this Directory as an advertising medium, and the opinion of the Council was invited concerning the propriety of members of the medical profession having their names advertised in this manner. The matter was fully discussed and the Council unanimously passed the following resolution—"That with reference to Percy and Dearsley's City Street Directory, wherein

[1] From the original in the Mitchell Library, Sydney.

special stress is laid in their circular on the value of it as an advertising medium, the Council wish to direct the attention of the members to the following By-law (No. 36): 'No member shall be a party to the appearance of a notice of his life in the public Press, or insert any advertisement beyond an announcement of a change of address, or commencement or resumption of practice' and to remind members that the insertion of their names in the Directory will be a breach of the By-law".

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Diploma Courses.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that courses will be held for the following four medical diplomas as follows:

Part I, for a period of eleven weeks from August 31 to November 13, 1959: D.A. (35 guineas), D.G.O. (50 guineas), D.L.O. (50 guineas), D.O. (50 guineas).

Part II, from November 16, 1959, to March, 1960: D.A. (40 guineas), D.G.O. (50 guineas), D.L.O. (50 guineas), D.O. (50 guineas).

Application for enrolment on these courses should be made to the Course Secretary, the Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney, from whom copies of the diploma regulations and other relevant information may be obtained. Telephones: BU 4497-8. Telegraphic Address: "Postgrad Sydney".

Course in Obstetrics and Gynæcology at The Women's Hospital, Crown Street.

The Post-Graduate Committee in Medicine in the University of Sydney announces that a course in obstetrics and gynæcology will be held at The Women's Hospital, Crown Street, Sydney, from Monday to Friday, August 31 to September 4, 1959, under the supervision of Dr. J. G. Harrington. Enrolments will be limited to 14 post-graduate students in residence and 12 attending as external students. The fees for attendance are £8 18s. 6d. (including board and residence) or £6 6s. (external attendance). Candidates may take up residence on Saturday afternoon, August 29, after 4 p.m. The programme is as follows:

Monday, August 31: 9.30 a.m., welcome by Dr. J. N. Chesterman; 9.40 a.m., "Management of Abnormal Presentation", Dr. F. A. Bellingham; 11.15 a.m., "Endometriosis", Dr. K. A. McGarrity; 2 p.m., symposium on "Abortion', chairman, Dr. H. A. McCredie; speakers: "Ætiology", Dr. R. Mackey; "Treatment of Incomplete Abortion", Dr. R. D. Macbeth; "Treatment of Threatened Abortion", Dr. W. G. McBride; 3.45 p.m., "Management of Labour" (with demonstrations), Dr. R. D. Macbeth.

Tuesday, September 1: 9.30 a.m., "Post-Menopausal Bleeding", Dr. S. Devenish Meares; 11.15 a.m., "Exchange Transfusion", Dr. S. E. L. Stening and Dr. R. H. Vines; 2 p.m., Sterility Clinic demonstration, Dr. R. Mackey and Dr. R. Bowman; 3.45 p.m., "Management of Labour" (with demonstrations), Dr. R. Mackey.

Wednesday, September 2: 9.30 a.m., "Recent Advances in Obstetrics and Gynæcology in the United Kingdom', Dr. R. B. C. Stevenson; 11.15 a.m., "Pelvic Cancer Clinic Cases and Demonstrations", Dr. J. N. Chesterman, Dr. R. B. C. Stevenson and Dr. W. G. McBride; 2 p.m., "Anæsthesia in Obstetrics", chairman, Dr. F. A. Bellingham; speakers, Dr. C. N. Paton, Dr. J. R. Radcliff, Dr. J. R. B. Beaumont; 3.45 p.m., symposium on "Bleeding in Late Pregnancy", chairman, Dr. H. A. McCredie; speakers: "Accidental Hæmorrhage', Dr. F. A. Bellingham; "Post-Partum Hæmorrhage", Dr. W. G. McBride; "Placenta Prævia", Dr. R. Bowman.

Thursday, September 3: 9.30 a.m., "Medical Complications of Pregnancy", Dr. Richmond Jeremy, Dr. F. Hales Wilson, Dr. Helen Taylor, Dr. T. I. Robertson; 11.15 a.m., "Manual Rotation and Forceps Delivery in the Management of Occipito-Posterior Presentation', Dr. R. D. Macbeth; 2 p.m., symposium on "Prolapse", chairman, Dr. H. A. McCredie; speakers: "Ætiology", Dr. K. A. McGarrity, "Complications", Dr. S. Devenish Meares, "Treatment", Dr. J. N. Chesterman; 3.45 p.m., "Management of Labour" (with demonstrations), Dr. M. Drummond.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JULY 4, 1959.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	2(1)	..	1	1	..	..	..	1	5
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	..	..	1	..	..	..	15	..	16
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	3(3)	14(12)	..	..	3(3)	..	3	1	24
Diphtheria	..	1(1)	..	..	3(3)	..	..	..	4
Dysentery (Bacillary)	..	11(11)	..	2(2)	2(2)	..	2	..	17
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	46(14)	13(5)	12(1)	7(3)	2(1)	..	..	..	80
Lead Poisoning	..	..	1(1)	..	..	..	..	..	1
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	1	..	..	..	..	..	1
Malaria	..	..	1	..	..	..	1	..	2
Meningococcal Infection	4(1)	1(1)	1	1(1)	..	..	..	..	7
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	1(1)	..	..	..	..	..	..	1
Puerperal Fever	2	1(1)	..	..	..	..	..	..	3
Rubella	..	18(14)	..	..	1(1)	..	..	..	19
Salmonella Infection	..	..	..	..	1(1)	..	..	..	1
Scarlet Fever	11(6)	18(16)	4	4(1)	1(1)	2(2)	..	1	41
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	..	..	..	..	..	..
Trachoma	..	..	..	..	6(6)	..	..	..	6
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	15(14)	18(13)	3(1)	10(8)	5(5)	6(3)	..	..	57
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	1	..	..	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Friday, September 4: 9.30 a.m., "Biopsy of the Cervix in Detection of Carcinoma", Dr. M. Drummond; 11.15 a.m., "Prolonged Labour", Dr. D. H. McGrath; 2 p.m., question time, chairman, Dr. J. N. Chesterman.

Written application, enclosing remittance for attendance as a resident or external student, should be made at an early date to the Course Secretary, The Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Enrolments will be made in order of receipt of fees, and the list will be closed as soon as the required number of applications is received. Telephones: BU 4497-8.

Post-Graduate Training in Cardio-Vascular Diseases.

The Post-Graduate Committee in Medicine in the University of Sydney announces its intention to introduce a running course in cardio-vascular diseases. This will comprise a series of courses dealing with various aspects of the subject suitable both for general practitioners and for post-graduates studying for higher degrees and diplomas. Each component of the course will take the form of four weekly evening lectures with panel discussions. The subjects will include hypertension, atherosclerosis, ischæmic heart disease, heart failure, heart disease in young subjects, rheumatic heart disease, cardiac investigations, electrocardiography and advances in therapy, and appropriate medical films will be shown. The fee for attendance will be £4 4s. for each group of four evenings. There will also be two short intensive week-end courses each year in electrocardiography (March) and in recent advances in cardiology (August). Plans are already well advanced for the establishment of a correspondence course in electrocardiography.

The first of the courses will consist of seminars on hypertension, to be held on the Wednesdays of October 7, 14, 21 and 28, 1959, from 8 to 10 p.m. Further details regarding the programme and location of these seminars will be announced shortly.

The Royal Australasian College of Physicians.

VICTORIAN STATE COMMITTEE.

Lecture by Professor C. R. B. Blackburn.

A MEETING of the Victorian Fellows and Members of The Royal Australasian College of Physicians will be held in the Lecture Theatre of the Royal Australasian College of Surgeons, Spring St., Melbourne, at 8.15 p.m. on Wednesday, September 2, 1959. Professor C. R. B. Blackburn, Department of Medicine, University of Sydney, will speak on "Physics in Physic".

All members of the medical profession are invited to be present.

College of Pathologists of Australia.

ANNUAL MEETING, 1959.

THE annual meeting of The College of Pathologists of Australia will be held on September 3, 4 and 5, 1959, in the Holme and Sutherland Rooms of the Union, University of Sydney. Scientific sessions will be held on Thursday, September 3, from 9.30 a.m. to 4.50 p.m., on Friday, September 4, from 9.30 a.m. to 12.50 p.m., and on Saturday, September 5, from 9.30 a.m. to 10.20 a.m. The annual general meeting will be held on Saturday, September 5, at 11 a.m. On Friday, September 4, from 2.30 to 5 p.m., a demonstration of a working auto analyser will be given in the Listerian Theatre, Old Medical School, University of Sydney.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Caldwell, Norman James, L.M.S.S.A. (London), 1944, M.R.C.S. (England), 1945, L.R.C.P. (London), 1945, D.P.H., R.C.P. & S. (England), 1950, Department of Public Health, 52 Bridge Street, Sydney.

Deaths.

THE following deaths have been announced:

POKORNY-ZSIGMOND.— Akos Pokorny-Zsigmond, on July 22, 1959, at Sydney.

FRY.—Henry Kenneth Fry, on July 22, 1959, at Waverley Ridge, Crafers, South Australia.

Diary for the Month.

AUGUST 11.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
AUGUST 13.—New South Wales Branch, B.M.A.: Public Relations Committee.
AUGUST 14.—Tasmanian Branch, B.M.A.: Branch Council.
AUGUST 14.—Queensland Branch, B.M.A.: Council Meeting.
AUGUST 15.—Victorian Branch, B.M.A.: Country Branch Meeting (Geelong).
AUGUST 17.—Victorian Branch, B.M.A.: Finance Subcommittee.
AUGUST 18.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales. Anti-Tuberculosis Association of New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

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